

# IUCT Oncopole

## 2 présentations posters 1<sup>er</sup> auteur

### An open-label, multicohort, phase I/II study to evaluate nivolumab in patients with virus-associated tumors (CheckMate 358): Efficacy and safety in recurrent or metastatic (R/M) nasopharyngeal carcinoma (NPC).

Sub-category:

[Advanced Disease](#)

Category:

Head and Neck Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

6025

Poster Board Number:

Poster Session (Board #13)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 6025)

Author(s): [Jean-Pierre Delord](#), Antoine Hollebecque, J. P. De Boer, Jacques De Greve, Jean-Pascal H. Machiels, Rom S. Leidner, Robert L. Ferris, Shangbang Rao, Ibrahima Soumaoro, Z. Alexander Cao, Hyunseok Kang, Suzanne Louise Topalian; [Toulouse University Cancer Institute IUCT-Oncopole, Toulouse, France](#); Gustave Roussy Cancer Institute, Villejuif, France; Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; Vrije Universiteit Brussel (VUB), Brussels, Belgium; Cliniques Universitaires Saint-Luc, Brussels, Belgium; Earl A. Chiles Research Institute, Portland, OR; University of Pittsburgh Medical Center Cancer Center Pavilion, Pittsburgh, PA; Bristol-Myers Squibb, Princeton, NJ; The Sidney Kimmel Comprehensive Cancer Center and Bloomberg-Kimmel Institute for Cancer Immunotherapy at Johns Hopkins, Baltimore, MD

#### [Abstract Disclosures](#)

Abstract:

**Background:** Treatment options for patients (pts) with R/M NPC are limited to palliative chemotherapy. NPC is often associated with the Epstein–Barr virus (EBV), a potential antigen for immune recognition, and high expression levels of the immune checkpoint receptor programmed death-1 (PD-1) and its major ligand PD-L1. Nivolumab disrupts PD-1–mediated signaling, restoring T-cell antitumor function. **Methods:** In CheckMate 358 (NCT02488759), PD-L1–unselected adults with R/M NPC, ECOG PS of 0–1, and ≤2 prior systemic therapies in the R/M setting were eligible to receive nivolumab 240 mg every 2 weeks until progression or unacceptable toxicity, as part of an ongoing multicohort study of 5 virus-associated cancers. Human papillomavirus-associated NPC and keratinizing squamous cell carcinoma (WHO Type 1) were excluded. Primary endpoints were objective response rate (ORR) and safety; secondary endpoints were duration of response (DoR), progression-free survival (PFS), and overall survival (OS). **Results:** Of 24 treated pts with R/M NPC, median age was 51 years, 88% were male, 62% were white, 88% were European, and 88% had EBV+ tumors. At a median follow-up of 26 weeks (range: 4–40), ORR was 20.8% and appeared to be higher in pts with no prior R/M therapy (Table). The disease control rate (ORR + SD) was 45.8%. Responses were observed regardless of PD-L1 or EBV status. Median PFS was 2.4 mo (95% CI: 1.5, NR); median OS was NR. **Conclusions:** Nivolumab demonstrated clinical activity and a manageable safety profile in R/M NPC, supporting ongoing research with nivolumab in this disease. Updated efficacy and biomarker data will be presented. Clinical trial information: [NCT02488759](#)

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**Response and safety.**

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	Response-evaluable pts (N = 24)	Prior systemic R/M therapies	
		0 (n = 5)	≥1 (n = 19)
<b>Best overall response, n (%)</b>			
Complete response	0	0	0
Partial response	5 (20.8)	2 (40.0)	3 (15.8)
Stable disease (SD)	6 (25.0)	2 (40.0)	4 (21.0)
Progressive disease	13 (54.2)	1 (20.0)	12 (63.2)
ORR, % (95% CI)	20.8 (7, 42)	40.0 (5, 85)	15.8 (3, 40)
Time to response, median (range), mo	4.4 (1.7, 5.7)		
DoR, median, mo	NR		
<b>Treatment-related adverse events, %</b>			
Any grade	54.2		
Grade 3–4	8.3		

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NR = not reached.

## Individualization of high dose carboplatin based on therapeutic drug monitoring (TDM) for the treatment of testicular germ cell tumors (TICE protocol): Results of a multicenter phase II study.

Sub-category:

[Germ Cell/Testicular](#)

Category:

Genitourinary (Nonprostate) Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

4554

Poster Board Number:

Poster Session (Board #232)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 4554)

Author(s): [Fabienne Thomas](#), Sotheara Moeung, Sophie Broutin, Jerome Guitton, Michele Boisdron-Celle, Joseph Ciccolini, Christophe Massard, Aude Flechon, Remy Delva, Gwenaelle Gravis, Jean-Pierre Lotz, Jacques-Olivier Bay, Marine Gross-Goupil, Angelo Paci, Vianney Poinsignon, Karim Fizazi, [Thierry Lafont](#), [Isabelle Lochon](#), [Christine Chevreau](#), [Etienne Chatelut](#); [Institut Claudius Regaud](#), [IUCT-Oncopole](#), [CRCT](#), [Inserm](#), [Toulouse](#), France; [Institut Gustave Roussy](#), [Villejuif](#), France; [Pharmacokinetic Department](#); [Hospices Civils de Lyon](#); [Centre Hospitalier Lyon-Sud](#), [Pierre-Benite](#), France; [Institut De Cancérologie De L'ouest - Site Paul Papin](#), [St Leger Des Bois](#), France; [Aix Marseille University](#), [Marseille](#), France; [Institut Gustave Roussy Cancer Centre](#), [Villejuif](#), France; [Centre Léon-Bérard](#), [Lyon](#), France; [Institut de Cancerologie de l'Ouest](#), [Angers](#), France; [Institut Paoli-Calmettes](#), [Marseille](#), France; [Medical Oncology Department](#), [Hospital Tenon \(AP-HP\)](#), [Paris](#), France; [Cellular Therapy and Clinic Hematology Unit for Adults](#), [Clermont-Ferrand](#), France; [Centre Hospitalier-Universitaire Saint Andre](#), [Bordeaux](#), France; [Gustave Roussy Cancer Campus](#), [Villejuif](#), France; [Department of Cancer Medicine](#), [Gustave Roussy Cancer Campus](#), [Paris-Sud University](#), [Villejuif](#), France; [IUCT-Oncopôle /Institut Claudius Regaud](#), [Toulouse](#), France; [Institut Claudius Regaud](#), [IUCT](#), [équipe n°14](#), [Université Paul Sabatier](#), [Toulouse](#), France

[Abstract Disclosures](#)

Abstract:

**Background:** We conducted a national phase II multicenter trial that aimed at evaluating the efficacy and tolerance of Paclitaxel plus Ifosfamide followed by high-dose carboplatin plus etoposide treatment (TICE) in previously treated germ cell tumors. The particularity of our study (in comparison with the standard protocol [Motzer RJ, et al. J Clin Oncol 2000 Mar; 18(6): 1173-1180.]) is that the carboplatin dose was individualized for each patient according to therapeutic drug monitoring (TDM) in order to reach the target AUC of 24 mg.min/ml over 3 days. **Methods:** In total, 89 patients were evaluable for pharmacokinetic study. Blood samples were taken on day 1 to determine the carboplatin clearance using a Bayesian approach (NONMEM 7.2) and to adjust the dose on day 3 to reach the target AUC of 24 mg.min/ml over 3 days. On days 2 and 3, samples were taken for retrospective assessment of the actual AUC and the intra- and inter-cycle clearance variability. Secondly, a population pharmacokinetic analysis was also performed on 59 patients using NONMEM to develop a covariate equation for carboplatin clearance prediction adapted for future patients treated with the TICE protocol. The performance of this new equation was then prospectively evaluated on the other 30 patients along with different methods of carboplatin clearance prediction. **Results:** TDM allowed us to control the carboplatin exposure with a mean actual AUC of 24.5 mg.min/ml (22.2 and 28.0 for 5<sup>th</sup> and 95<sup>th</sup> percentile respectively) per cycle. We observed a modest but significant decrease of carboplatin clearance over cycles (median value of change of -11.8% from cycle 1 to cycle 3, maximum value of -36%). The new covariate equation allows unbiased and more accurate prediction of carboplatin clearance in the prospective validation cohort compared to other equations. **Conclusions:** Carboplatin TDM allowed the target AUC to be accurately reached and thereby avoid over- or under-exposure. We propose a new equation to predict carboplatin clearance more adapted to these particular patients (young males) that could be used as an alternative if the TDM cannot be organized. Clinical trial information: 2008-005068-14.

## 32 Participations posters

### Baseline frequency of brain metastases and outcomes with multikinase inhibitor therapy in patients with *RET*-rearranged lung cancers.

Sub-category:

[Metastatic Non-Small Cell Lung Cancer](#)

Category:

Lung Cancer—Non-Small Cell Metastatic

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

9069

Poster Board Number:

Poster Session (Board #395)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 9069)

Author(s): Alexander E. Drilon, [Thomas Filleron](#), Isabella Bergagnini, Julie Milia, Vaios Hatzoglou, Vamsidhar Velcheti, Benjamin Besse, Tony Mok, Mark M. Awad, Juergen Wolf, David P. Carbone, D. Ross Camidge, Gregory J. Riely, Nir Peled, [Julien Mazieres](#), Mark G. Kris, Oliver Gautschi, Global Multicenter RET Registry Investigators; Memorial Sloan Kettering Cancer Center, New York, NY; [Institut Universitaire du Cancer - Oncopole, Toulouse, France](#); Memorial Sloan-Kettering Cancer Center, New York, NY; [Hôpital Larrey Centre Hospitalier Universitaire Toulouse, Toulouse, France](#); Memorial Sloan-Kettering Cancer Center and Weil Cornell Medical College, New York, NY; Cleveland Clinic Taussig Cancer Institute, Cleveland, OH; Gustave Roussy Cancer Campus, Villejuif, France; Chinese University of Hong Kong, Hong Kong, China; Massachusetts General Hospital, Cambridge, MA; Lung Cancer Group Cologne, Center for Integrated Oncology, University Hospital Cologne, Cologne, Germany; The Ohio State University Comprehensive Cancer Center, Columbus, OH; University of Colorado-Denver, Aurora, CO; Davidoff Cancer Center, Petah Tikva, Israel; Cantonal Hospital Lucerne, Luzern, Switzerland

#### [Abstract Disclosures](#)

Abstract:

**Background:** In phase 2 trials, multikinase inhibitors with activity against RET are active in a subset of patients (pts) with *RET*-rearranged lung cancers (response rate of 28%, phase 2 study of cabozantinib; Drilon et al Lancet Oncol 2016). Data on the incidence of brain metastases and outcomes with multikinase inhibitor therapy in pts with intracranial disease have not previously been reported. **Methods:** The frequency of brain metastases at diagnosis of metastatic disease was evaluated in pts accrued to a global registry of *RET*-rearranged lung cancer pts identified by a multicenter network of thoracic oncologists (Gautschi et al JCO 2017). A proportion of pts were treated with 9 multikinase inhibitors including cabozantinib, vandetanib, lenvatinib, alectinib, and ponatinib. On a prospective phase 2 trial (NCT01639508), patients with asymptomatic brain metastases were eligible. Intracranial response to cabozantinib (RECIST v1.1) was evaluated in an exploratory fashion. **Results:** 114 registry pts with *RET*-rearranged lung cancers had metastatic disease at diagnosis. Baseline brain metastases were identified in 27% (95%CI 18-34%, n = 20/75) of pts with available information. No differences (p > 0.05) in age, smoking history, or upstream fusion partner (*KIF5B* 100% vs 84%, with and without brain metastases, p = 0.53) were noted. In 37 pts treated with multikinase inhibitors with activity against RET, there were no significant differences in median PFS (2.1 vs 2.1 months, p = 0.41) or median OS (3.9 vs 7.0 months, p = 0.10) in pts with (n = 10) and without (n = 27) brain metastases. On a phase 2 trial of cabozantinib, baseline untreated brain metastases were present in 5 pts. Intracranial disease control (stable disease; -34% and -1% in 2 pts with measurable disease) was achieved in 4 of 4 pts with measurable or evaluable intracranial disease with time to treatment discontinuation ranging from 2.4 months to 2.9 years. **Conclusions:** Brain metastases are present in a substantial proportion of *RET*-rearranged lung cancer pts. Intracranial disease control can be achieved in select pts by a multikinase inhibitor. Novel RET-directed targeted therapy strategies should address intracranial disease. Clinical trial information: [NCT01639508](#)

### Pre-operative tomotherapy for retroperitoneal liposarcoma: Results of a phase II multicenter study.

Sub-category:

[Bone Tumors](#)

Category:

Sarcoma

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

e22501

Citation:

J Clin Oncol 35, 2017 (suppl; abstr e22501)

Author(s): Guy Kantor, Eberhard Stoeckle, [Martine Delannes](#), Marc-Andre Mahe, Antoine Italiano, Michèle Kind, Christine Dupouy, Antoine Giraud, Mikael Antoine, Maud Toulmonde, Augustin Mervoyer, [Gwennael Ferron](#), Carine A. Bellera, Paul Sargos; Institut Bergonié, Department of Radiation Therapy, Bordeaux, France; Institut Bergonié, Department of Surgery, Bordeaux, France; [Institut Claudius Regaud, IUCT-Oncopôle, CRCT, Inserm, Toulouse, France](#); Institut de Cancérologie de l'Ouest - René Gauducheau, Nantes, France; Institut Bergonié, Bordeaux, France; Institut Bergonié, Department of Imaging, Bordeaux, France; Institut Bergonié, Department of Medical Oncology, Bordeaux, France; Institut de Cancérologie de l'Ouest - René Gauducheau, Radiation Therapy Department, Saint-Herblain, France; [IUCT-Oncopôle /Institut Claudius Regaud](#), Toulouse, France; Clinical and Epidemiological Research Unit, Institut Bergonié, Comprehensive Cancer Centre, Bordeaux, France

#### [Abstract Disclosures](#)

Abstract:

**Background:** To evaluate efficacy and feasibility of radiotherapy (RT: high-level dose 54 Gy, with 30 fractions over / 6 weeks) followed by surgery, for retroperitoneal liposarcomas. **Methods:** Helical tomotherapy was used for pre-operative RT. Clinical Target Volume (CTV) and main organs at risk were systematically delineated with the surgeon. Surgery was planned 4 to 8 weeks after RT. Inclusion criteria were operable, biopsy-proven, retroperitoneal liposarcomas. Toxicity was graded according to CTCAE V3.0. Overall survival (OS) was estimated using Kaplan-Meier method. Due to competing risks, we estimated the cumulative incidence of loco-regional relapse; 95% confidence intervals are reported [95%CI]. **Results:Patients:**From 04/2009 to 09/2013, 48 patients were included. Mean age: 62 years (y) (36 to 82). All but 1 patient were OMS  $\leq$  2. Histological types were 20 well differentiated (WDLS) and 28 dedifferentiated liposarcomas. Mean CTV was 2954 cc. **Treatment:**1 patient did not have surgery. Dosimetric constraints were respected. Monobloc exeresse was systematically achieved. Surgical margins were R0 (16; 34%), R1 (28; 60%), R2 (2; 4%) or missing (1; 2%). **Oncological outcomes:**Median follow-up was 4.7 y. Cumulative incidence of loco-regional relapse at 3 and 5 y was 17% [8%; 29%] and 31% [16%; 47%] respectively. Estimates were 5% and 35% for dedifferentiated liposarcoma and 26% and 26% for well differentiated liposarcoma. OS at 3 and 5 y was 81% [66%; 89%] and 78% ([63%; 88%] respectively. **Toxicity:** 2 months after surgery, 10 grade 3 toxicities and 1 grade 4 toxicity were reported for 6 patients; 3 patients died within 6 months after surgery, 2 of which were related to treatment. After 1 y, no further severe toxicity was observed; 5 cases of second cancers were reported: 1 myeloid leukaemia, 2 pancreatic, 2 breast carcinomas. **Conclusions:** This trial highlights the feasibility of preoperative 54 Gy RT. Although efficacy data (local control and OS) are encouraging, high incidence rates of acute toxicities and second cancers should be considered. Preoperative RT for WDLS remains questionable. Results from ongoing EORTC phase III Strass trial may provide further level of evidence for this approach. Clinical trial information: [NCT01841047](#)

## Pembrolizumab therapy for microsatellite instability high (MSI-H) colorectal cancer (CRC) and non-CRC.

Sub-category:

[Immune Checkpoint Inhibitors](#)

Category:

Developmental Therapeutics—Immunotherapy

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

3071

Poster Board Number:

Poster Session (Board #166)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 3071)

Author(s): Luis A. Diaz, Aurelien Marabelle, [Jean-Pierre Delord](#), Ronnie Shapira-Frommer, Ravit Geva, Nir Peled, Tae Won Kim, Thierry Andre, Eric Van Cutsem, [Rosine Guimbaud](#), Dirk Jaeger, Elena Elez, Takayuki Yoshino, Andrew K. Joe, Baohong Lam, Christine K. Gause, Scott Knowles Pruitt, S. Peter Kang, Dung T Le; Memorial Sloan Kettering Cancer Center, New York, NY; Gustave Roussy, Université Paris-Saclay, Villejuif, France; [Institut Claudius Regaud, IUCT-Oncopôle, CRCT, Inserm, Toulouse, France](#); Chaim Sheba Medical Center, Ramat Gan, Israel; Tel Aviv Sorasky Medical Center, Tel Aviv, Israel; Davidoff Cancer Center, Petah Tikva, Israel; Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; Medical Oncology Department, Saint-Antoine Hospital, Paris, France; University Hospitals Leuven, Leuven, Belgium; University Hospital of Rangueil, Toulouse, France; Department of Medical Oncology, National Center for Tumor Diseases, Heidelberg University Hospital, Heidelberg, Germany; Vall d'Hebron University Hospital, Barcelona, Spain; Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital, Chiba, Japan; Merck & Co., Inc., Kenilworth, NJ; Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD

## Abstract Disclosures

### Abstract:

**Background:** Mismatch repair deficient cancers harbor high levels of microsatellite instability and somatic mutations. Treatment with anti-PD-1 antibodies has resulted in durable objective responses in MSI-H cancer. As part of the ongoing, global, multicenter phase 2 studies KEYNOTE(KN)164 and KN158, we assessed the efficacy of pembrolizumab in patients (pts) with MSI-H tumors. **Methods:** Both studies enrolled pts with MSI-H status determined locally by IHC or PCR. KN164 enrolled pts with MSI-H CRC and  $\geq 2$  prior therapies, whereas the multicohort KN158 study included pts with MSI-H non-CRC and  $\geq 1$  prior therapy. Eligible pts in both studies received pembrolizumab 200 mg Q3W until progression, unacceptable toxicity, or pt/investigator decision. Tumor response was assessed every 9 wk by independent review per RECIST v1.1. Primary endpoint was ORR. Secondary endpoints included DOR, PFS, OS, and safety. Analyses were performed in pts from KN164 and KN158 who had  $\geq 27$  wk of follow-up as of Aug 3, 2016 and Oct 19, 2016, respectively. **Results:** KN164 enrolled 61 pts with MSI-H CRC (90% with  $\geq 2$  prior therapies) whereas KN158 included 21 pts with MSI-H non-CRC (42% with  $\geq 2$  prior therapies). In KN158 the most common tumor types were endometrial and small intestinal cancer (n = 4 each), cholangiocarcinoma (n = 3), and gastric and pancreatic cancer (n = 2 each). Median follow-up was 7.4 mo for MSI-H CRC and 4.5 mo for MSI-H non-CRC. ORR for MSI-H CRC was 26.2% (95% CI, 15.8%-39.1%), with 15 confirmed responses and 1 unconfirmed response, and ORR for MSI-H non-CRC was 42.9% (21.8%-66.0%), with 8 confirmed responses and 1 unconfirmed response. DCR was 50.8% (n = 31; 37.7%-63.9%) for MSI-H CRC and 66.7% (n = 14; 38.4%-83.7%) for MSI-H non-CRC. Median duration of response was not reached for either MSI-H CRC or non-CRC, and 100% of responses were ongoing. Survival and safety analyses are ongoing. **Conclusions:** Early results from KN164 and KN158 confirm the robust antitumor activity of pembrolizumab in heavily pretreated pts with MSI-H cancers. Clinical trial information: [NCT02628067](#); [NCT02460198](#)

## Carfilzomib weekly-melphalan-prednisone in untreated elderly multiple myeloma: IFM2012-03.

Sub-category:

[Multiple Myeloma](#)

Category:

Hematologic Malignancies—Plasma Cell Dyscrasia

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

8004

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 8004)

Author(s): Xavier Leleu, Guillemette Fouquet, Lionel Karlin, Brigitte Kolb, Mourad Tiab, Carla Araujo, Murielle Roussel, Pascal Bourquard, Pascal Lenain, Catherine Humbrecht-Kraut, Karim Belhadj, Marie-Odile Petillon, Marie-Lorraine Chretien, Philippe Rodon, Olivier Decaux, Arnaud Jaccard, Cyrille Hulin, [Michel Attal](#), Philippe Moreau, Thierry Facon; CHU, Poitiers, France; Hematology, CHRU Lille, Lille, France; Centre Hospitalier Lyon-Sud, Pierre-Bénite, France; University Hospital, Reims, France; CH, La Roche Sur Yon, France; Centre Hospitalier de la Cote Basque, Bayonne, France; Cancer Research Center, Toulouse, France; CHU Nîmes, Department of Haematology, Nîmes, France; Hématologie, Centre Henri Becquerel, Rouen, France; CH Colmar, Colmar, France; Hôpital Henri Mondor, Créteil, France; CHRU Lille, Lille, France; CHU Dijon, Dijon, France; CH Périgueux, Périgueux, France; University Hospital, Rennes, France; Centre Hospitalier Universitaire de Limoges - Hôpital Dupuytren, Limoges, France; Bordeaux Hospital University Center (CHU), Bordeaux, France; [Hôpital Purpan, Toulouse, France](#); CHU de Nantes-Hôtel Dieu, Nantes, France; Service des Maladies du Sang, Hôpital Claude Huriez, Lille, France

## Abstract Disclosures

### Abstract:

**Background:** Melphalan-prednisone-bortezomib (MPV) is a standard of care upfront for newly diagnosed elderly myeloma (eNDMM). Despite significant improvements on MPV's safety profile, toxicity issues remain. Carfilzomib (K) is a novel generation proteasome inhibitor with a different safety profile from Bortezomib. Carmysap phase I/II study (twice a week Carfilzomib+MP) demonstrated K at 36mg/m<sup>2</sup> safe and active in eNDMM. We thought to study the K weekly-MP combination in eNDMM. **Methods:** IFM2012-03 is a multicenter phase I/II study in eNDMM (65 and older) aimed to determine the maximum tolerated dose (MTD) of K weekly. 4 cohorts of 6 patients each were recruited at K 36, 45, 56 and 70 mg/m<sup>2</sup> on days 1, 8, 15, 22 IV of 35-days cycles, with oral Melphalan and Prednisone from days 1 to 4 at usual doses. Patients received a 9-cycles induction followed by a K monotherapy

maintenance at 36 mg/m<sup>2</sup> IV every 2 weeks for 1 year. 3 dose-limiting toxicities (DLTs) defined MTD at the lower N-1 dose. **Results:** 24 patients were included at K 36, 45, 56 and 70 mg/m<sup>2</sup>. One DLT occurred at 36 mg/m<sup>2</sup> (grade 4 lymphopenia), one at 45 mg/m<sup>2</sup> (tumor lysis syndrome with grade 4 renal insufficiency), two at 56 mg/m<sup>2</sup> (grade 3 cardiac insufficiency and grade 3 febrile neutropenia) and two at 70 mg/m<sup>2</sup> (grade 3 nausea/vomiting and grade 3 hepatic cytolysis). One patient died from cardiac dysfunction considered related to K at 56 mg/m<sup>2</sup>. 3 patients stopped therapy and 3 others required dose reduction of K. Following DSMB's request a second 6-patients cohort was recruited at 70 mg/m<sup>2</sup>, with increased attention around hyperhydration and monitoring HTA. We observed no DLT and no grade 3/4 adverse event in this cohort. Median age was 75 years, 56% patients were R-ISS 2 or 3. For the whole cohort (N=30), the overall response rate was 87% including 67% very good partial responses and 44% complete responses. **Conclusions:** The MTD of weekly K in the KMP combination is 70 mg/m<sup>2</sup> upfront for eNDMM, but it seems reasonable to recommend 56mg/m<sup>2</sup> after 75 years-old for safety reasons. KMP offers high response rates and possibly greater CR rate. However, since the CLARION study (VMP vs KMP) will not allow KMP's approval in eNDMM in Europe, IFM decided to stop IFM2012-03 after phase I without performing phase II. Clinical trial information: [NCT02302495](https://clinicaltrials.gov/ct2/show/study/NCT02302495)

## **PREDICTOR (UNICANCER GEP11): Randomized phase II study of preoperative afatinib in untreated head and neck squamous cell carcinoma (HNSCC) patients.**

Sub-category:

[Biomarkers/Epidemiology/Outcomes](#)

Category:

Head and Neck Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

6021

Poster Board Number:

Poster Discussion Session (Board #9)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 6021)

Author(s): Christophe Le Tourneau, [Jean-Pierre Delord](#), Gilles Dolivet, Olivier Malard, Jérôme Fayette, Olivier Capitain, Caroline Even, Caroline Hoffmann, [Sebastien Vergez](#), Lionnel Geoffrois, Frederic Rolland, Philippe Zrounba, Laurent Laccourreye, Joel Guigay, Ivan Bieche, Jerzy Klijanienko, Nicolas Aide, Valerie Benavent, Jocelyn Gal, Stephane Temam; Institut Curie - Centre de Lutte Contre le Cancer (CLCC) de Paris, Paris, France; [Institut Claudius Regaud, IUCT-Oncopole, CRCT, Inserm, Toulouse, France](#); Institut de Cancérologie de Lorraine, Vandoeuvre-Les-Nancy, France; CHU de Nantes, Nantes, France; Medical Oncology, Centre Léon Bérard, Lyon, France; Institut de Cancerologie de l'Ouest, Angers, France; Institut Gustave Roussy, Villejuif, France; Institut Curie, Paris, France; Department of Head and Neck Surgery, [Institut Claudius Regaud, Toulouse, France](#); [Centre Alexis Vautrin, Vandoeuvre-Lès-Nancy, France](#); Department of Medical Oncology, Institut de Cancérologie de l'Ouest, Nantes, France; Department of Head and Neck Surgery, Centre Léon Bérard, Lyon, France; CHU d'Angers, Angers, France; Department of Medical Oncology, Antoine Lacassagne Comprehensive Cancer Centre, FHU Oncoage, Nice, France; Department of Nuclear Medicine, Centre François Baclesse, Caen, France; Unicancer, Paris, France; Centre Antoine Lacassagne, Nice, France; Department of Head and Neck Surgery, Gustave Roussy, Villejuif, France

[Abstract Disclosures](#)

Abstract:

**Background:** Afatinib, a pan-HER irreversible tyrosine kinase inhibitor, demonstrated limited antitumor activity compared to methotrexate in unselected recurrent and/or metastatic HNSCC patients (LUX-HN1, Machiels et al, Lancet Oncol 2015). The UNICANCER (GEP 11) PREDICTOR study's objective was to identify predictive and pharmacodynamic biomarkers of biological activity and efficacy of afatinib (EUDRACT N° 2010-024046-29). **Methods:** This open-label, randomized, multicentric, controlled, phase II study included untreated patients with operable T2-4N0-2M0 HNSCC of the oral cavity, pharynx and larynx, with a PS < 2, adequate organ function and LVEF > 50%. Patients were randomized (2:1) to: oral afatinib (A) 40mg/day (d) for 14-28d or no treatment (NT). Patients had pre-treatment tumor biopsies, tumor imaging, and PET CT scan, with a 2<sup>nd</sup> tumor imaging before surgery and a PET scan at D15. Adverse events were classified by NCI CTCAE criteria. Based on the biological primary endpoint of tumor reduction the sample size was designed to identify biomarkers associated with a 20% difference between the study arms. **Results:** 61 patients were included (A: 41/NT: 20). 2 patients in the NT arm were not analyzed (consent withdrawal, no surgery). 7 patients in arm A received < 14d of treatment, including 6 patients with unacceptable toxicity. Afatinib-related toxicities were: grade (G)1 37%, G2 41%, G3 7%, G4 5%, and G5 0%. G≥3 toxicities were mainly gastrointestinal. Partial responses (RECIST1.1) were observed in 3 patients (7.3%) in arm A versus none in the NT arm (p = 0.018). Progressive disease was not observed in arm A versus 3 (16.6%) in the NT arm. Partial responses on PET CT scan by PERCIST were observed in 15/31 evaluable patients (48%) in arm A versus 1/15 (6.7%) in the NT arm (p = 0.005). **Conclusions:** Afatinib given to

HNSCC patients in the preoperative setting is safe and is associated with improved response according to RECIST1.1 and PERCIST compared to no treatment. Clinical trial information: [NCT01415674](#)

## Specific adaptive immune pattern induced by NBTXR3 exposed to radiation therapy in soft tissue sarcoma (STS) patients.

Sub-category:

[Inflammatory Signatures](#)

Category:

Developmental Therapeutics—Immunotherapy

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

e14615

Citation:

J Clin Oncol 35, 2017 (suppl; abstr e14615)

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[Abstract Disclosures](#)

Abstract:

**Background:** NBTXR3 are functionalized hafnium oxide nanoparticles, undergoing seven clinical trials for enhancing radiation therapy (RT). The high electron density of the nanoparticles, when exposed to radiotherapy (NBTXR3 + RT), allow absorption/deposition of a high radiation dose within the cancer cells to physically kill the cells, and possibly improve outcome. Besides, NBTXR3 + RT has shown subsequent ability to enhance immunogenic cell death and immune response in preclinics. We hypothesized that NBTXR3 + RT could trigger an enhanced immune response when compared to RT in patients with STS. **Methods:** Tumor tissues pre- (biopsy) and/or post-treatment (resection) were collected from patients (pts) with locally advanced STS, who received either NBTXR3 as intratumor injection and RT (14 pts) or RT (12 pts), as preoperative treatment (NCT02379845). Immunohistochemistry and Digital Pathology for immune biomarkers and for Immunoscore (CD3/CD8) were analyzed. Gene expression profiling and pre-optimized immune-gene signatures called Immunosign were also used. **Results:** A significant increase of T cells (CD3+, CD8+) and a marked increase of CD103+ immune cell infiltration post- vs pre-treatment were observed for NBTXR3 + RT ( $P < 0.01$ ), while no differences were seen for RT. Post-treatment, an increased Immunoscore (CD3 + CD8 cell densities) was observed for NBTXR3 + RT compared to RT ( $P < 0.07$ ). Consistently, the up-regulation of pan immune genes expression and specifically expression of adaptive immunity genes between pre- and post-treatment, was pronounced for NBTXR3 + RT when compared to RT. Functional analysis of genes up-regulated in NBTXR3 + RT showed an enrichment of cytokine activity (IL7, IFNA, IL16, IL11, IFNG), adaptive immunity (RAG1, GZMA, TAP1, TAP2, TBX21, STAT4, IFNG, LCK, LTK, CD37, CD22) and T cell receptor signaling pathway (CD28, CTLA4, CD274, BTLA, TIGIT, CD40LG, CD5, CD3E, ZAP70). **Conclusions:** NBTXR3 + RT induces a specific adaptive immune pattern. As such, it may contribute to convert “cold” tumor into “hot” tumor and be effectively combined with immunotherapeutic agents across oncology. These data warrant more tissue samples evaluation to reinforce these findings.

## Dose escalation of radiotherapy (RT) for locally advanced head and neck carcinomas treated with concomitant chemotherapy (CT) and RT: Results of the GORTEC 2004-01 randomized trial.

Sub-category:

[Local-Regional](#)

Category:

Head and Neck Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

6015

Poster Board Number:

Poster Discussion Session (Board #3)



Citation:

J Clin Oncol 35, 2017 (suppl; abstr 6015)

Author(s): Jean Bourhis, Anne Auperin, Marc Alfonsi, xu Shan Sun, [Michel Rives](#), Yoann Pointreau, Cedrik Lafond, Pierre Boisselier, [Pierre Graff](#), Juliette Thariat, Yungan Tao, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; Institut Gustave Roussy, Villejuif, France; Institut Sainte-Catherine, Avignon, France; CHRU Jean Minjot, Besancon Cedex, France; [Institut Claudius Regaud, IUCT-Oncopole, CRCT, Inserm, Toulouse, France](#); Centre Hospitalier et Régional Universitaire, Henry S. Kaplan Center, Clinique d'Oncologie et de Radiothérapie, Tours, France; Clinique Victor Hugo, Le Mans, France; Institut du Cancer de Montpellier, Montpellier, France; Centre Antoine Lacassagne, Nice, France

#### [Abstract Disclosures](#)

Abstract:

**Background:** Concomitant CT-RT is a well established standard of care (SoC) in locally advanced (LA) squamous cell carcinomas of the head and neck (SCCHN). While there is a well established dose effect relationship for RT alone in these cancers, it is not known whether this also applies to concomitant CT-RT. **Methods:** Patients were randomized between 75 Gy/7 weeks (Arm A) versus 70 Gy/35F in 7 weeks (Arm B). A sequential boost of 10 times 2.5 Gy after 50Gy/25F was given to the initial gross tumor volume (GTV) in Arm A. IMRT was used for arm A and 3D conformal RT for arm B. In both arms, patients (pts) received during RT 3 cycles of cisplatin at 100 mg/m<sup>2</sup>. Inclusion criteria were pts fit for receiving high dose cisplatin, non metastatic, non operated stage III-IV SCC of oral cavity, oro/hypopharynx. A 1:1 randomization was done by minimization on centers, N & T stages & GTV uni/bilateral. To detect a hazard ratio (HR) of 0.56 in locoregional (LR) control, inclusion of 310 pts was required to observe 109 LR progressions and achieve 85% power at 2-sided significance level of 0.05. **Results:** Between 2005 and 2015, 188 pts were randomized: 82% males, median age 58 years, 85% oropharynx. The accrual rate was slower than expected, due to the fact that IMRT became a SoC and was only allowed in arm A. As a consequence the trial was discontinued after inclusion of 188 patients. The majority of pts had stage IVa (73% vs 72%). All initial characteristics were well balanced between arms. The median follow-up was 4.7 years, not different between arms. Acute and late xerostomia were markedly improved in arm A (IMRT arm). The 1-year grade 0-1 salivary toxicity (RTOG) was 81% and 34% (p< 0.0001) in arm A and B respectively. At 3 years these rates were 92% vs 53% (p=0.0003). The increase of the dose to the GTV with IMRT did not transfer in a higher LR control probability with an adjusted HR of 0.88 [95%CI 0.51-1.52] (p=0.63). PFS, overall survival were not significantly different between the 2 arms. **Conclusions:** The dose escalation of RT to the GTV did not improve LR control in patients treated with concomitant CT-RT. This trial adds some new evidence level 1 in favor of IMRT in LA SCCHN. Clinical trial information: [NCT00158678](#)

## The benefit of combining docetaxel to androgen deprivation therapy in localized and metastatic castration-sensitive prostate cancer as predicted by ERG status: An analysis of two GETUG phase III trials.

Sub-category:

[Biomarkers/Epidemiology/Outcomes](#)

Category:

Genitourinary (Prostate) Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

5012

Poster Board Number:

Poster Discussion Session (Board #86)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 5012)

Author(s): Shanna Rajpar, Alexandra Carmel, Zahira Merabet, Philippe Vielh, Stéphanie Foulon, Francois Lesaunier, Remy Delva, Frederic Rolland, Frank Priou, Jean-Marc Ferrero, Nadine Houede, [Loic Mourey](#), Christine Theodore, Ivan Krakowski, Laura Faivre, Muriel Habibian, Stephane Culine, Anne Chauchereau, Gwenaëlle Gravis, Karim Fizazi; Institut Gustave Roussy, Villejuif, France; Gustave Roussy Cancer Institute, Villejuif, France; Gustave Roussy Cancer Campus, Villejuif, France; Centre François Baclesse, Caen, France; Centre Paul Papin, Angers, France; Department of Medical Oncology, Institut de Cancérologie de l'Ouest, Nantes, France; Centre Hospitalier Départemental Vendée, La Roche-Sur-Yon, France; Department of Medical Oncology, Centre Antoine-Lacassagne, Nice, France; Centre Hospitalier Régional Universitaire, Nîmes, France; [Institut Claudius Regaud, IUCT-Oncopole, CRCT, Inserm, Toulouse, France](#); Hospital Foch, Suresnes, France; Institut Bergonié, Bordeaux, France; Gustave Roussy, Villejuif, France; Federation Nationale des Centres de Lutte Contre le Cancer, Paris, France; Medical Oncology Department, Hospital Saint-Louis, Paris, France; Institut Gustave Roussy Inserm U981, Villejuif, France; Institut Paoli-Calmettes, Marseille, France; Gustave Roussy Cancer Campus and University Paris-Sud, Villejuif, France

#### [Abstract Disclosures](#)

Abstract:

**Background:** Combining docetaxel to androgen deprivation therapy (ADT) improves survival in metastatic castration-sensitive prostate cancer (CSPC) (Vale C, Lancet Oncol 2016; 17: 243-56) and it also improves relapse-free survival (RFS) in high-risk localized CSPC (Fizazi K, Lancet Oncol 2015; 16: 787-94). However it is unlikely that all patients (pts) derive a

benefit from docetaxel treatment and identifying predictive biomarkers remains a major unmet need. A subset of prostate cancers contains TMPRSS2-ERG gene fusions leading to ERG overexpression. **Methods:** Pre-treatment prostate core biopsies were collected from 255/413 pts and 79/385 pts enrolled respectively in the GETUG 12 and GETUG 15 (Gravis G, Eur Urol 2016; 70: 256-62) phase 3 trials testing early docetaxel in high-risk localized and metastatic CSPC. ERG, PTEN, Ki67 and Rb expression was assessed using immunohistochemistry. RFS curves were compared using the Logrank test. **Results:** The median age was 63 years (46-77) and 62 years (49-76) in GETUG 12 and GETUG 15. ERG staining was positive in 88/191 (46%) and 33/79 (42%) pts with available tissue, respectively. In GETUG 12, docetaxel-based chemotherapy was associated with improved RFS in pts with ERG+ expression (HR = 0.55 [0.29-1.03]; 6-year RFS : 80% ADT+docetaxel vs 68% ADT alone), but not in pts with ERG- (HR = 1.10 [0.66-1.85]; 6-year RFS 55% ADT+docetaxel vs 60% ADT alone), interaction test: p = 0.02. Similar findings were observed in GETUG 15, which was used as a validation set: the median RFS was 10.7 (6.5-14.3) and 18.8 (9.8-41) months in pts with ERG+ cancers receiving ADT alone and ADT+docetaxel, and 10.6 (4.8-25.3) and 13.2 (9.4-24) months in pts with ERG- cancers. In contrast, no difference in patient outcome by docetaxel treatment was observed by PTEN, Ki67 and Rb expression. **Conclusions:** Docetaxel-related benefit in men with CSPC is predicted by ERG expression. This biomarker may help better select pts for docetaxel treatment.

## Assessment of multiple endocrine therapies for metastatic breast cancer in a multicenter national observational study.

Sub-category:

[Hormone Receptor-Positive](#)

Category:

Breast Cancer—Metastatic

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

1052

Poster Board Number:

Poster Session (Board #44)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 1052)

Author(s): Olivia Le Saux, Audrey Lardy-Cleaud, Sophie Frank, Paul H. Cottu, Barbara Pistilli, Marc Debled, Laurence Vanlemmens, Marianne Leheuteur, Anne-Valérie Guizard, Lilian Laborde, Lionel Uwer, Veronique D'hondt, [Delphine Berchery](#), Veronique Lorgis, Jean-Marc Ferrero, Genevieve Perrocheau, Coralie Courtinard, Sylvie Chabaud, Mathieu Robain, Thomas Denis Bachelot; Centre Léon-Bérard, Lyon, France; Institut Curie, Paris, France; Institut Gustave Roussy, Villejuif, France; Institut Bergonié, South-West Comprehensive Cancer Center, Bordeaux, France; Centre Oscar Lambret, Lille, France; Centre Henri Becquerel, Rouen, France; Centre François Baclesse, Caen, France; IPC, Marseille, France; Centre Alexis Vautrin, Nancy, France; Institut du Cancer de Montpellier, Montpellier, France; [IUCT-Oncopôle /Institut Claudius Regaud, Toulouse, France](#); Centre Georges-François Leclerc, Dijon, France; Department of Medical Oncology, Centre Antoine-Lacassagne, Nice, France; ICO René Gauducheau, Saint-Herblain, France; Unicancer, Paris, France

### Abstract Disclosures

Abstract:

**Background:** For HR+/HER2- metastatic breast cancer (mBC), International guidelines recommend multiple lines of endocrine therapy (ET) before starting chemotherapy. Few studies have assessed the efficacy of such strategy on large populations. Our objective was to evaluate multiple ET activity according to clinical and biological characteristics and type of ET. **Methods:** All patients (pts) who initiated treatment for a newly diagnosed mBC between January 2008 and December 2014 in all 18 French Comprehensive Cancer Centers were included in the real life ESME database. ESME collects retrospective data using a clinical trial-like methodology. Database lock was 8 Dec 2016. Primary endpoint of the current study was progression free survival (PFS) on successive ET lines. Only pts with ET alone were assessed (pts receiving ET after chemotherapy as maintenance therapy, or combined with targeted treatment were excluded). **Results:** 9921 pts out of 16703 in ESME, had HR+/HER2- mBC (median age 62.0 years[range 23-96]). 53.9% of pts had visceral and 80.1% non visceral disease at diagnosis. Median OS of HR+/HER2- pts was 42.15 months (95% CI, 40.93-43.27). As first-line therapy, 4123 pts (41.6%) received ET alone, while 2038 received chemotherapy alone (20.5%) and 3667 received both (37%). Median PFS for first-line ET (N=4123) was 11.3 months (95% CI, 10.6-11.9). Only 668 pts (16%) received subsequent lines of ET alone. Types of ET used are described in the table below. Successive PFS will be reported at the meeting. **Conclusions:** Those data show that ET is prescribed to less than 50% of patients with HR+/HER2- mBC in first line and only to a small minority in subsequent lines. This is not in line with existing guidelines (NCCN, ABC3). Real-life median PFS for first-line ET is consistent with median PFS reported in clinical trials (Nabholtz, 2000).

Endocrine therapy (ET)	First-line N=4123	Subsequent lines N=668
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Endocrine therapy (ET)	First-line N=4123	Subsequent lines N=668
Non steroidal aromatase inhibitors (AI)	2868 (69.6%)	299 (44.7%)
Steroidal AI	749 (18.2%)	196 (29.3%)
Selective Estrogen Receptor Modulator	929 (22.5%)	214 (32.0%)
Selective Estrogen Receptor Degradar	562 (13.6%)	288 (43.0%)
LHRH Analogs	339 (8.2%)	33 (4.9%)
Other	33 (0.8%)	20 (3.0%)

Type of ET prescribed.

## A phase III, randomized, open-label study of isatuximab (SAR650984) plus pomalidomide (Pom) and dexamethasone (Dex) versus Pom and Dex in relapsed/refractory multiple myeloma.

Sub-category:

[Multiple Myeloma](#)

Category:

Hematologic Malignancies—Plasma Cell Dyscrasia

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

TPS8057

Poster Board Number:

Poster Session (Board #380a)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr TPS8057)

Author(s): Paul G. Richardson, [Michel Attal](#), Jesus San Miguel, Frank Campana, Solenn Le-Guenec, Ai-Min Hui, Marie-Laure Risse, Kenneth Carl Anderson; Dana-Farber Cancer Institute, Boston, MA; [Institut Universitaire du Cancer - Oncopole, Toulouse, France](#); Clinica Universidad de Navarra, Pamplona, Spain; Sanofi Oncology, Cambridge, MA; Sanofi, Vitry-Sur-Seine, France; Sanofi-Genzyme Oncology, Cambridge, MA; Sanofi R&D, Vitry-Alfortville, France

[Abstract Disclosures](#)

Abstract:

**Background:** Treatment for refractory or relapsed and refractory multiple myeloma (MM) remains an unmet need. Isatuximab (ISA), an anti-CD38 monoclonal antibody with multiple mechanisms of tumor killing, has shown efficacy and an acceptable tolerability profile in Phase 1/2 studies in patients with refractory or relapsed and refractory MM (RRMM) (Richter et al. ASCO 2016; Vij et al. ASCO 2016). **Methods:** This Phase III, prospective, multicenter, randomized, open-label study (NCT02990338; ICARIA-MM) is being conducted to evaluate the clinical benefit of ISA in combination with Pom and low-dose Dex (Pom/Dex) versus Pom/Dex for the treatment of adult patients with RRMM and demonstrated disease progression within 60 days of the last therapy, and who have received at least 2 prior lines of therapy, including lenalidomide and a proteasome inhibitor (bortezomib, carfilzomib, or ixazomib) alone or in combination. Patients will be randomly assigned in a 1:1 ratio to either ISA (10 mg/kg IV on Days 1, 8, 15, and 22 in the 1st cycle; Days 1 and 15 in subsequent cycles) plus Pom (4 mg on Days 1–21) and Dex (40 mg for patients < 75 years of age and 20 mg for patients ≥75 years of age, on Days 1, 8, 15, and 22) or Pom and Dex. Treatment cycles will be 28 days each. Patients will continue therapy until disease progression, occurrence of unacceptable adverse events (AEs), or their decision to discontinue the study, whichever comes first. The primary endpoint is progression-free survival (PFS), i.e. time from randomization to progressive disease or death from any cause. Response will be determined by IMWG criteria (2016). Key secondary endpoints include overall response rate and overall survival (OS). Safety evaluations include treatment-emergent AEs/serious AEs (including infusion-associated reactions), laboratory parameters, vital signs and assessment of physical examination. Statistical analyses will be conducted according to a pre-specified plan; approximately 300 patients (150 in each arm) are expected to be enrolled in this study. The first patient was recruited in January 2017. Study funding: Sanofi. Clinical trial information: [NCT02990338](#)

## Efficacy of daratumumab in combination with lenalidomide plus dexamethasone (DRd) or bortezomib plus dexamethasone (DVd) in relapsed or refractory multiple myeloma (RRMM) based on cytogenetic risk status.

Sub-category:

[Multiple Myeloma](#)

Category:

Hematologic Malignancies—Plasma Cell Dyscrasia

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

8006

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 8006)

Author(s): Katja C. Weisel, Jesus San Miguel, Gordon Cook, Merav Leiba, Kenshi Suzuki, Shaji Kumar, Michele Cavo, [Herve Avet-Loiseau](#), Hang Quach, Vania Hungria, Suzanne Lentzsch, Roman Hajek, Pieter Sonneveld, Kaida Wu, Xiang Qin, Christopher Chiu, David Soong, Ming Qi, Jordan Mark Schecter, Meletios A. Dimopoulos; Universitaetsklinikum Tuebingen der Eberhard-Karls-Universitaet, Abteilung fuer Innere Medizin II, Tuebingen, Germany; Clinica Universidad de Navarra, Pamplona, Spain; St James's Institute of Oncology, Leeds Teaching Hospitals NHS Trust and University of Leeds, Leeds, United Kingdom; Sheba Medical Center, Ramat Gan, Israel; Japanese Red Cross Medical Center, Tokyo, Japan; Division of Hematology, Mayo Clinic, Rochester, MN; Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Bologna, Italy; [Unité de Génomique du Myélome, CHU Rangueil, Toulouse, France](#); University of Melbourne, St. Vincent's Hospital, Victoria, Australia; Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, Brazil; Division of Hematology/Oncology, Columbia University, New York, NY; University Hospital Ostrava and Faculty of Medicine and Faculty of Science, University of Ostrava, Ostrava, Czech Republic; Erasmus Medical Center, Rotterdam, Netherlands; Janssen Research and Development, LLC, Spring House, PA; Janssen Research and Development, LLC, Raritan, NJ; Janssen Research and Development, LLC, Raritan, NY; National and Kapodistrian University of Athens School of Medicine, Athens, Greece

### Abstract Disclosures

Abstract:

**Background:** In 2 randomized phase 3 trials of RRMM patients (pts), DRd (POLLUX) or DVd (CASTOR) significantly improved PFS and deepened responses compared with Rd or Vd alone, respectively. The novel mechanism of action of daratumumab (D) may improve the poor prognosis associated with high-risk cytogenetic abnormalities in RRMM. Therefore, we examined the efficacy of DRd and DVd among RRMM pts with standard (std) or high cytogenetic risk status. **Methods:** Bone marrow aspirates were collected at screening and assessed centrally via next generation sequencing (NGS). Pts with high-risk cytogenetics included those who had  $\geq 1$  of the following abnormalities: t(4;14), t(14;16), or del17p; std-risk pts were defined as those confirmed negative for these abnormalities. Efficacy analyses included PFS and ORR. **Results:** Samples from 311/569 pts in POLLUX and 353/498 pts in CASTOR were assessed via NGS. In POLLUX, the median duration of follow-up was 17.3 months. Significantly longer median PFS and numerically higher ORR were observed with DRd vs Rd among high-risk patients, and significant improvements in these outcomes were observed in std-risk patients (Table). In CASTOR, the median duration of follow-up was 13.0 months. Significantly longer median PFS and higher ORR were observed with DVd vs Vd among both high- and std-risk pts (Table). Concordance rates for t(4;14), t(14;16), and del17p were high (88%-98%) between NGS and FISH. Updated data, including subgroup analyses, will be presented. **Conclusions:** In RRMM pts, the addition of D to standard-of-care regimens improved outcomes regardless of cytogenetic risk status. Targeting CD38 by combining D with Rd or Vd appears to improve the poor outcomes associated with high-risk cytogenetic status. See table. Clinical trial information: [NCT02136134](#) and [NCT02076009](#)

	POLLUX				CASTOR			
	High		Std		High		Std	
	DRd (n=28)	Rd (n=37)	DRd (n=133)	Rd (n=113)	DVd (n=44)	Vd (n=51)	DVd (n=123)	Vd (n=135)
NGS								
Median PFS, mo	NR	10.2	NR	17.1	11.2	7.2	NR	7.0
HR (95% CI)	0.44 (0.19-1.03)		0.30 (0.18-0.49)		0.49 (0.27-0.89)		0.29 (0.20-0.43)	
P	0.0475		<0.0001		0.0167		<0.0001	

NGS	POLLUX				CASTOR			
	High		Std		High		Std	
	DRd (n=28)	Rd (n=37)	DRd (n=133)	Rd (n=113)	DVd (n=44)	Vd (n=51)	DVd (n=123)	Vd (n=135)
ORR, %	85	67	95	82	82	62	85	64
<i>P</i>	0.14		0.0020		0.039		0.0003	
≥CR, %	33	6	52	24	30	9	25	8
≥VGPR, %	63	31	84	51	64	34	64	27

## Triple-NOTE (Triple Negative Outcome in ESME): Large recent real-world prognostic data on triple negative metastatic breast cancers (mTNBC).

Sub-category:

[Triple-Negative](#)

Category:

Breast Cancer—Metastatic

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

e12592

Citation:

J Clin Oncol 35, 2017 (suppl; abstr e12592)

Author(s): Marie-Paule Sablin, Corinne Tchokothe, Delphine Loirat, Thomas Denis Bachelot, Emmanuelle Fourme, Matthieu Carton, Meriem Mokdad-Adi, [Delphine Berchery](#), Christelle Levy, William Jacot, Frederique Madeleine Penault-Llorca, Anthony Goncalves, Laurence Vanlemmens, Jean-Christophe Eymard, Mario Campone, Gaetane Simon, Mathieu Robain, Christian Cailliot, Christophe Le Tourneau, Francesco Ricci; Institut Curie, Paris, France; Centre Léon-Bérard, Lyon, France; Institut Curie, Saint-Cloud, France; Gustave Roussy, Villejuif, France; [IUCT-Oncopôle /Institut Claudius Regaud, Toulouse, France](#); Centre François Baclesse, Caen, France; Institut du Cancer de Montpellier, Montpellier, France; Centre Jean Perrin, Clermont-Ferrand, France; Department of Medical Oncology, Institut Paoli-Calmettes, Marseille, France; Centre Oscar Lambret, Lille, France; Institut Jean-Godinot, Reims, France; Institut de Cancérologie de l'Ouest - René Gauducheau, Saint-Herblain, France; Unicancer, Paris, France

### Abstract Disclosures

Abstract:

**Background:** During last decade, therapeutic arsenal has expanded for metastatic breast cancer (mBC), but few data are available about mTNBC, a poor prognosis subtype. In 2014, UNICANCER (composed of 18 French Comprehensive Cancer Centers) launched the Epidemiological Strategy and Medical Economics (ESME) program to centralize real-world data. This base represents a great opportunity to update the outcomes and the treatment practice patterns of this population. **Methods:** The ESME-mBC database was built from information systems, treatment databases and patients' electronic files including quality control processes. All pts who initiated treatment for mBC between 01-Jan-2008 and 31-Dec-2014 were selected. The primary objective of this study was to assess overall survival (OS) of mTNBC pts. TNBC status was defined as ER and PR < 10% in both primary and metastatic disease, as well as the absence of overexpression or amplification of HER2. The secondary objectives were to describe the characteristics of this population, clinical management (duration and sequence of treatments) and to evaluate the prognostic value of several clinical factors (age, distant disease free interval, location and number of metastatic sites) **Results:** Among 16703 pts in the ESME-mBC database, 2368 (14%) had mTNBC. Median OS over this time period was 14.8 months (95% CI 14-15.6). Median age at diagnosis of mBC was 57 years. For the pts who relapsed, median metastasis free interval was 24 months, while 25.5% of the pts were *de novo* metastatic. 61% of the pts presented visceral metastasis and 12% had cerebral metastasis as first metastatic site. The pattern of metastatic involvement (visceral and cerebral) and a short metastasis free interval (< 24 months) were the most important prognostic factors in multivariate analysis. The description of treatment sequences (duration, prognostic value) will be presented. **Conclusions:** In this real-life setting database, mTNBC remain of poor prognosis despite a trend for a better OS than the historical data available (12-13 ms). This TNBC ESME cohort is one of the largest available and offers an updated assessment of the outcomes of this population.

## The role of PET for predicting nodal response in locally advanced (LA) head and neck squamous cell carcinoma (HNSCC) treated with chemoradiotherapy (CRT): Results of a prospective multicenter trial.

Sub-category:

[Local-Regional](#)

Category:

Head and Neck Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

6013

Poster Board Number:

Poster Discussion Session (Board #1)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 6013)

Author(s): Sandra Schmitz, Aline Van Maanen, Laura Rousseaux, Guy Andry, Stéphane Temam, Didier Dequanter, [Sebastien Vergez](#), Benjamin Lallemand, Dominique De Raucourt, Franck Jegoux, Francois-Xavier Hanin, Vincent Gregoire, Marc Hamoir; Department of Head and Neck Surgery, St-Luc Hospital, Catholic University of Louvain, Brussels, Belgium; Institut Roi Albert II, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium; Saint-Luc Hospital, Brussels, Belgium; Institut Bordet, Brussels, Belgium; Institut Gustave Roussy, Villejuif, France; CHU Charleroi, Charleroi, Belgium; Department of Head and Neck Surgery, [Institut Claudius Regaud, Toulouse, France](#); Centre Hospitalier de Nimes, Nimes, France; CAC de Caen, Caen, France; CHU Rennes, Rennes, France; Department of Nuclear Medicine, St-Luc Hospital, Catholic University of Louvain, Brussels, Belgium; Cliniques Universitaires Saint-Luc, Brussels, Belgium

### [Abstract Disclosures](#)

Abstract:

**Background:** Controversy about neck management after CRT in patients with LA HNSCC persists due to low accuracy of CT/MR to assess the neck. As already demonstrated (Mehanna, NEJM 374, 2016), PET is an alternative to planned neck dissection (ND) thanks to its high negative predictive value (NPV). However, no conclusion could be drawn for patients (pts) with equivocal response (e.g. suspicion of residual disease on CT/MR but negative PET) because pathologic confirmation was lacking. **Methods:** Multicenter, prospective, nonrandomized trial including pts with LA HNSCC of oral cavity, oro- hypopharynx, larynx, staged N1, N2, N3, treated with CRT and evaluated 12 weeks after CRT by overall assessment (OA): clinical examination (CE), PET and CT/MR. ND was performed in incomplete regional response based on at least 1 positive evaluation method. Pathologic analyses (HE and KI67) were performed on ND samples. Primary objective was to determine the NPV and accuracy of PET as a single examination in the post CRT nodal assessment. Primary outcome was 2-year regional recurrence free survival rate (RRFSR). **Results:** 264/318 pts included completed full treatment and had post CRT OA. Median follow up was 40 months. No ND was proposed in 119 patients because of a negative OA; 145 patients had ND. The presence of viable cells was reported in 27 ND (18.6%). Sensitivity, specificity, PPV, NPV, accuracy of OA were 90.0%, 49.6%, 18.6%, 97.5%, 54.2% vs 69.7%, 75.3%, 28.8%, 94.6%, 74.6% for PET alone. Kappa coefficient was of 0.838, indicating an almost perfect agreement. In pts with negative OA, RRFSR was 61.3% vs. 56.6% in pts with positive OA and ND (p=0.45). Using post CRT assessment with PET alone, RRFSR in pts with negative PET was 63.0% vs. 48.8% in pts with positive PET (p=0.04). Using PET assessment alone, 65/145 ND (44.8%) could have been avoided without compromising RRFSR. **Conclusions:** NPV using PET alone is 94.6%. Post CRT evaluation using only PET would have resulted in considerably fewer ND without jeopardizing neck control. PET alone is more accurate and more discriminant for predicting pts outcome. Clinical trial information: [NCT00634777](#)

## Long-term survival (over 10 years) of inoperable/metastatic GISTs: A retrospective series of 141 patients (pts) of the french sarcoma group (FSG).

Sub-category:

[Gastrointestinal Stromal Tumors \(GIST\)](#)

Category:

Sarcoma

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

11041

Poster Board Number:

Poster Session (Board #364)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 11041)

Author(s): Florence Duffaud, Edouard Auclin, Antoine Italiano, Julien Mancini, Francois Bertucci, Nicolas Penel, Marc Pracht, Guillaume Vogin, Olivier Collard, Emmanuelle Bompas, Bruno Landi, [Thibaud Valentin](#), Loic Chaigneau, Maud Toulmonde, Antoine Adenis, Isabelle Laure Ray-Coquard, Maria Rios, S Bastien Salas, Axel Le Cesne, Jean-Yves Blay, French Sarcoma Group; Hopital de la Timone, Marseille, France; Medical and Gastrointestinal Oncology Department, Georges Pompidou Hospital; Methodology and Quality of Life Unit in Oncology (INSERM UMR 1098), University Hospital of Besançon, Paris, France; Institut Bergonié, Bordeaux, France; University Hospital La Timone, Marseille, France; Institut Paoli-Calmettes, Marseille, France; Centre Oscar Lambret, Lille, France; Service d'Oncologie Médicale, Centre Eugene Marquis, Rennes, France; Institut de Cancérologie de Lorraine, Département de Radiothérapie, Vandoeuvre-Les-Nancy, France; Institut de Cancérologie de la Loire, St. Priest en Jarez, France; Centre René Gauducheau, Nantes, France; Hospital European Georges Pompidou, Clamart, France; [Oncopole, Toulouse, France](#); Institut Regional du Cancer en Franche-Comté - University Hospital, Besançon, France; Institut Bergonié, Department of Medical Oncology, Bordeaux, France; Centre Léon-Bérard, Lyon, France; Centre Alexis Vautrin, Nancy, France; Gustave Roussy Cancer Campus, Villejuif, France

#### [Abstract Disclosures](#)

Abstract:

**Background:** A subset of metastatic GIST exhibit very long-term survival after imatinib (IM) introduction. The aim of this study was to analyse the clinico-biological characteristics of GIST pts alive > 10 years (yrs) after diagnosis (dx) of metastases (mets) and identify possible factors associated with long-term survival. **Methods:** Pts were identified from 2 sarcoma databases; NetSarc and ConticaGIST. Clinical data prospectively registered in the databases were supplemented with retrospective review of medical records. **Results:** We identified 141 pts (75 men, 66 women) with median age 54 (17-84) yrs and median ECOG 0 (0-2). Primary tumors (T) were all CD117+, and mainly gastric or intestinal (64 & 45 pts), with median size 10 (2-40) cm, CD34+ (82 pts), mitoses/50 HPF  $\leq 5$  (n = 36), or  $> 5$  (n = 81). Genotype was documented in 82 (58%) pts with 73 (89%) *KIT* mutations (in exons 11,9 and 12 of 69, 3, and 1 pts respectively) and 9 WT *KIT*. 129 (91%) T were resected, 124 upfront, 5 post IM, with R0/R1/R2 resections in 61, 11, and 10 pts. Mets were mainly hepatic or peritoneal (78 & 51 respectively). 1<sup>st</sup> line TKI was given to 139 pts: 130 received IM; 88 (63%) within a clinical trial (CT), 41 (29%) had mets resection. Second, 3<sup>d</sup> and 4<sup>th</sup> line TKI were given to 81, 51 and 37 pts respectively, comprising 27, 7 and 10 from CT. Median number of TKIs was 2 (0-7), but 60 (44%) pts received only 1<sup>st</sup> line with no GIST progression within or after 10 yrs. 2 pts never received TKI but had mets resection. After median FU of 14.3 yrs (10-34.5), 104 remain alive, 37 died. Mean and Median OS from initial dx are 24 yrs (CI95% 21.6-27) and 20,8 yrs. Median PFS on TKIs are 127, 29, 21 and 22 mos on 1<sup>st</sup>, 2<sup>d</sup>, 3<sup>d</sup> and 4<sup>th</sup> line of TKI. In univariate analysis no factor is significantly associated with OS, but T size ( $\leq 10$  vs  $> 10$  cm) and oligometastatic disease ( $\leq 5$  vs  $> 5$  mets) are borderline significant (p = 0.056 and 0.07), and good PS (ECOG  $\leq 1$ ) at 2<sup>d</sup>line TKI initiation is associated with better PFS (p = 0.03). **Conclusions:** This large series of long-term (> 10 yrs) survivors of metastatic GIST shows a high proportion of mets resection and a longer duration of PFS for TKI at any line. In this selected population, no prognostic factor is associated with long OS.

## Outcomes based on age in the phase 3 METEOR trial of cabozantinib (cabo) vs everolimus (eve) in patients with advanced renal cell carcinoma (RCC).

Sub-category:

[Kidney Cancer](#)

Category:

Genitourinary (Nonprostate) Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

4578

Poster Board Number:

Poster Session (Board #256)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 4578)

Author(s): Frede Donskov, Robert J. Motzer, Eric Voog, Elizabeth J. Hovey, Carsten Grulich, Louise M. Nott, Katharine Ellen Cuff, Thierry Gil, Niels Viggo Jensen, [Christine Chevreau](#), Sylvie Negrier, Reinhard Depenbusch, Lothar Bergmann, Izzy Cornelio, Anne Champsaur, Bernard J. Escudier, Sumanta K. Pal, Thomas Powles, Toni K. Choueiri; Aarhus University Hospital, Aarhus, Denmark; Memorial Sloan-Kettering Cancer Center, New York, NY; Centre Jean Bernard, Le Mans, France; Prince of Wales Hospital, Sydney, Australia; National Center for

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#### **Abstract Disclosures**

##### **Abstract:**

**Background:** The incidence of RCC increases with age with the highest incidence at ~75 years of age (Znaor, Eur Urol 2015). The Phase 3 METEOR trial (NCT01865747) showed a significant improvement in progression-free survival (PFS; HR 0.58, 95% CI 0.45–0.74;  $P < 0.0001$ ), overall survival (OS; HR 0.66, 95% CI 0.53–0.83,  $P = 0.0003$ ), and objective response rate (ORR; 17% vs 3%;  $P < 0.0001$ ) for cabo compared with eve in patients with advanced RCC previously treated with VEGFR TKIs (Choueiri, NEJM 2015, Lancet Oncol 2016). Here we present outcomes by 3 categories of age for the METEOR trial. **Methods:** 658 patients were randomized 1:1 to cabo (60 mg qd) or eve (10 mg qd). Stratification factors were MSKCC risk group and number of prior VEGFR TKIs. Endpoints included PFS, OS, and ORR. Subgroup analyses by age ( $< 65$ , 65 to 74, and  $\geq 75$  years) are presented. **Results:** At baseline, 60% of patients were  $< 65$  years old, 31% were 65 to 74 years old, and 10% were  $\geq 75$  years old. Subgroups by age generally had similar baseline characteristics in both arms. The HRs for PFS favored cabo for all age groups (HR 0.53, 95% CI 0.41–0.68 for  $< 65$  years old; 0.53, 95% CI 0.37–0.77 for 65 to 74 years old; and 0.38, 95% CI 0.18–0.79 for  $\geq 75$  years old). ORR per independent radiology committee for cabo vs eve was 15% vs 5% for  $< 65$  years old, 21% vs 2% for 65 to 74 years old, and 19% vs 0% for  $\geq 75$  years old. HRs for OS also favored cabo (HR 0.72, 95% CI 0.54–0.95 for  $< 65$  years old; 0.66, 95% CI 0.44–0.99 for 65 to 74 years old; and 0.57, 95% CI 0.28–1.14 for  $\geq 75$  years old). Median OS for cabo vs eve was 21.4 mo vs 17.1 mo for  $< 65$  years old, not reached vs 18.0 mo for 65 to 74 years old, and 18.4 mo vs 14.0 mo for  $\geq 75$  years old. Older patients more frequently had dose reductions (60% with cabo and 22% with eve for  $< 65$  years old vs 85% with cabo and 36% with eve for  $\geq 75$  years old). Grade 3 or 4 adverse events were generally consistent with the safety profiles in the overall population although some events such as fatigue and hypertension occurred at a higher rate in older patients. **Conclusions:** Treatment with cabo improved PFS, ORR, and OS compared with eve in patients with advanced RCC irrespective of age. Adverse events in older patients were more frequently managed with dose reductions. Clinical trial information: [NCT01865747](#)

## **Undifferentiated endometrial sarcomas (UES): Results of a French sarcoma group (FSG) retrospective series of 52 patients (pts).**

Sub-category:

[Uterine Cancer](#)

Category:

Gynecologic Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

e17109

Citation:

J Clin Oncol 35, 2017 (suppl; abstr e17109)

Author(s): Marie Meurer, Anne Floquet, Antoine Italiano, Morgane Auriche, Julien Mancini, Nicolas Penel, Isabelle Laure Ray-Coquard, [Martine Delannes](#), Sophie Piperno-Neumann, Francois Bertucci, Sébastien Salas, Jean-Yves Blay, Patricia Pautier, Florence Duffaud; Centre Hospitalier Universitaire La Timone, Marseille, France; Institut Bergonié, Bordeaux, France; Institut Gustave Roussy, Villejuif, France; University Hospital La Timone, Marseille, France; Centre Oscar Lambret, Lille, France; Centre Léon-Bérard, Lyon, France; [Institut Universitaire du Cancer - Oncopole, Toulouse, France](#); Medical Oncology, Institut Curie, Paris, France; Institut Paoli-Calmettes, Marseille, France; AP-HM, Marseille, France; GINECO and Gustave Roussy Cancer Center, Villejuif, France; La Timone University Hospital, Marseille, France



## Abstract Disclosures

### Abstract:

**Background:** UES are rare tumors of very poor prognosis. Although large surgical resection is the cornerstone of curative intent treatment, the optimal post-operative strategy remains unclear. **Methods:** We conducted a retrospective analysis of UES pts over the last 8 years in 10 FSG centers, from Netsarc and RRePs databases. **Results:** Fifty-two pts with primary UES treated from 2008 to 2016 were included. The median age was 59 years (range, 42-82), and median ECOG was 0 (range, 0-3): 33 were localized (FIGO I-III) and 19 metastatic at diagnosis. Metrorrhagia, abdominal pain, and pelvic mass bleeding were the most common symptoms. Surgical procedures were radical hysterectomy and bilateral adnexectomy for 23/33 (70%) of localized and 11/19 (58%) of metastatic UES. Metastases were identified post operatively for 9/19 pts. In the localized group, 19 pts (58%) received radiotherapy, 10 (30%) complementary brachytherapy and 9 (27%) adjuvant chemotherapy. In the metastatic group, 16/19 (84%) received chemotherapy (polyCT, n=11). With a median follow-up of 28 months (0.3-112), 24/52 pts are alive, 18/33 (58%) localized pts relapsed with 6 local relapses and 11 metastases. The 3- and 5-year Overall Survival (OS) rates were 40.7% and 29.1% respectively, for the whole group. In the localized group; median OS and Relapse-Free Survival (RFS) were 32.7 (23.3-42.1) and 22.9 months (2.3-43.7). In univariate analysis; early FIGO stage ( $p < 0.0001$ ), complete resection (R0-R1 vs R2;  $p=0.015$ ) and adjuvant radiotherapy ( $p=0.001$ ) were associated with a better OS; complete resection ( $p=0.021$ ) and adjuvant radiotherapy ( $p=0.026$ ) were associated with a better RFS. In the metastatic group, median OS was 16.4 months (12.0-20.7). In univariate analysis, no significant prognostic factor was retrieved neither on OS nor on RFS. **Conclusions:** Treatment of primary UES is radical hysterectomy and bilateral adnexectomy. Adjuvant radiotherapy appears beneficial for RFS. Due to the rarity and complexity of UES, referring patients to expert sarcoma centers is highly recommended.

## SHIVA: Randomized phase II trial comparing molecularly targeted therapy based on tumor molecular profiling versus conventional therapy in patients with refractory cancer—Overall survival (OS) analysis.

Sub-category:

[Molecular Diagnostics and Imaging](#)

Category:

Tumor Biology

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

11515

Poster Board Number:

Poster Discussion Session (Board #215)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 11515)

Author(s): Sylvain Dureau, Francesco Ricci, Marie Alt, Delphine Loirat, Marie-Paule Sablin, Maud Kamal, Ivan Bieche, Sebastien Armanet, [Jean-Pierre Delord](#), Anthony Goncalves, Celine Gavaille, Coraline Dubot, Nicolas Isambert, Mario Campone, Olivier Tredan, Miguella Marous, Aurelien Latouche, Lisa Belin, Christophe Le Tourneau; Institut Curie, Paris, France; Medical Oncology, Institut Curie, Paris, France; [Institut Claudius Regaud](#), [IUCT-Oncopole, CRCT, Inserm, Toulouse, France](#); Department of Medical Oncology, Institut Paoli-Calmettes, Marseille, France; Institut de Cancérologie de Lorraine, Département d'Oncologie Médicale, Nancy, France; Curie Institute, Saint Cloud, France; Centre Georges-François Leclerc, Dijon, France; Institut de Cancérologie de l'Ouest - René Gauducheau, Saint-Herblain, France; Département d'Oncologie Médicale, Centre Léon Bérard, Lyon, France; CNAM, Paris, France

## Abstract Disclosures

### Abstract:

**Background:** The SHIVA trial is a multicentric randomized phase II trial comparing molecularly targeted therapy among 11 drugs based on tumor molecular profiling versus conventional therapy in patients with any type of cancer that is refractory to standard of care (NCT01771458). Only patients who had a druggable molecular alteration (DMA) identified on a mandatory tumor sample from a metastatic site using targeted sequencing, CGH and IHC were randomized. Cross-over was allowed at disease progression. The trial did not show any difference for its primary endpoint (PFS) [*Le Tourneau et al., Lancet Oncol 2015*]. We report here the OS of randomized and non-randomized patients. **Methods:** OS was estimated in the 4 following groups: 1) randomized patients, 2) patients for whom a DMA was identified but who were not subsequently randomized because they did not meet the randomization criteria (PS of 0 or 1, adequate organ function), 3) non-randomized patients because of the absence of DMA, and 4) non-randomized patients because no genomic analyses were performed. Since 70% of patients randomized into the standard arm eventually crossed over to the targeted therapy arm, all randomized patients were analyzed in group 1. The groups were compared in terms of patient characteristics using student and  $\chi^2$  tests. OS was estimated using the Kaplan Meier method. **Results:** Among 741 patients included in SHIVA, 8 patients were included twice. Follow-up data were available for 680 out of the 733 patients. 197, 78, 222 and 183 patients belonged to groups 1 to 4, respectively. Median OS of the whole cohort was 7.9 months [95% CI:

7.0–9.1]. As compared to non-randomized patients due to the absence of identified DMA, non-randomized patients with a DMA had a significantly worse prognosis: HR = 2.3 [95% CI: 1.7–3.0] ( $p > 0.0001$ ) whereas randomized patients had a non-significant trend toward a better prognosis: HR = 0.85 [95% CI: 0.7–1.1] ( $p = 0.18$ ). **Conclusions:** A statistically significant difference in OS was only observed in patients with a DMA who were not randomized. However, our analysis does not allow showing an intrinsic prognostic value of the DMA on OS.

## Expression and prognostic significance of PDGF ligands (A, B, C, and D) and PDGFR (A, B, and L) in soft-tissue sarcomas and GIST.

Sub-category:

[Soft Tissue](#)

Category:

Sarcoma

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

11067

Poster Board Number:

Poster Session (Board #390)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 11067)

Author(s): Tom Lesluyes, Jean-Yves Blay, Patrick Schoffski, Antoine Italiano, Axel Le Cesne, Maria Debiec-Rychter, Olivier Mir, Raf Sciot, Maud Toulmonde, Isabelle Laure Ray-Coquard, Maria Rios, Mehdi Brahmi, [Christine Chevreau](#), Nicolas Isambert, Sylvie Bonvalot, Sophie Piperno-Neumann, Jean-Michel Coindre, Frederic Chibon; Institut Bergonié, Bordeaux, France; Centre Léon-Bérard, Lyon, France; Department of General Medical Oncology Leuven Cancer Institute, University Hospitals Leuven, KU Leuven, Leuven, Belgium; Gustave Roussy Cancer Campus, Villejuif, France; University Hospitals Leuven and Catholic University of Leuven, Leuven, Belgium; Gustave Roussy, Villejuif, France; Department of Pathology, KU Leuven and University Hospitals Leuven, Leuven, Belgium; Institut Bergonié, Department of Medical Oncology, Bordeaux, France; Centre Alexis Vautrin, Nancy, France; [IUCT-Oncopôle /Institut Claudius Regaud, Toulouse, France](#); Centre Georges-François Leclerc, Dijon, France; Institut Curie, Paris, France; Medical Oncology, Institut Curie, Paris, France; Institut Bergonié, Department of Pathology, Bordeaux, France

### Abstract Disclosures

Abstract:

**Background:** Sarcomas are a variety of rare connective tissue cancers. Doxorubicin and olaratumab (Ab against PDGFRA) improved survival in a recent Phase 1/2 study. Besides PDGFRA mutated gastrointestinal stroma tumor (GIST) and dermatofibrosarcoma protuberans, the role of PDGFR and the according ligands in the biology of sarcoma remain unclear. **Methods:** The expression levels of PDGF (A,B,C,D) and PDGFRs (A,B,L) were studied in a series of 255 sarcoma pts in localized phase using the Agilent 014850 platform. Data are available online (<http://atg-sarc.sarcomabcb.org>). Histologies were GIST (n = 60), myxoid liposarcoma (MLPS, n = 50), synovial sarcoma (SyS, n = 58), and sarcoma with complex genomics (SCG, n = 87). Expression levels were analyzed and tested for prognostic values for metastasis free survival (MFS) in uni- and multivariate analysis using SPSS 19.0. **Results:** Expression levels (ELs) of *PDGFs* and *PDGFRs* varied across histotypes: *PDGFA* levels were highest in SyS and lowest in MLPS ( $p < 0.0001$ ). *PDGFB* and *C* levels were lower in GIST ( $p < 0.0001$ ), while *PDGFD* ELs were similar across histological subtypes. *PDGFRA* ELs were highest in MLPS, while *PDGFRB* & *L* ELs were lowest in GIST and SyS ( $p < 0.0001$  all). Complex patterns of correlation of expression between ligands and receptors were observed in each individual subtypes. *PDGFA* ELs above median were associated with a marginally higher risk of metastasis. Conversely, *PDGFD* ELs above median was associated with a reduced risk of metastasis in the whole cohort ( $p = 0.02$ ). The ELs of the 3 receptors were not correlated to MFS. In multivariate analysis using Cox model on the non-GIST sarcoma cohort (histology, grade, depth, with size, *PDGFA*, *PDGFD* as continuous variables): histology, size, grade and *PDGFA* ELs were independent adverse prognostic factors (PF), while *PDGFD* ELs was a favorable PF for MFS. In the GIST cohort, testing AFIP score, *PDGFA* & *D* ELs as continuous variable, *PDGFD* ELs was also an independent favorable PF for MFS, in addition to AFIP score. **Conclusions:** The expression of PDGFs and the according receptors varies across sarcoma histological subtypes. *PDGFA* and *D* expression levels correlate independently to the risk of metastatic relapse.

## Follow-up of patients with complete remission of locally advanced basal cell carcinoma treated with vismodegib after treatment discontinuation: A retrospective multicentric French study.

Sub-category:

[Advanced Disease](#)

Category:

Melanoma/Skin Cancers

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

9535

Poster Board Number:

Poster Session (Board #143)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 9535)

Author(s): Florian Herms, Luc Haudebourg, Martine Bagot, Caroline Dutriaux, Jean Jacques Grob, Bernard Guillot, Geraldine Jeudy, Jérôme Lambert, Celeste Lebbe, Christine Mateus, [Nicolas Meyer](#), Sandrine Monestier, Laurent Mortier, Nicolas Poulalhon, Sorilla Prey, Caroline Robert, Pierre Vabres, Mehdi Mouri, Nicole Basset-Seguini; CHU Saint Louis, Paris, France; Dermatology, CHU Saint-André, Bordeaux, France; Aix-Marseille University and APHM Hospital CHU Timone, Marseille, France; Dermatology, CHU Montpellier, Montpellier, France; CHU Dijon, Dijon, France; Institut Gustave Roussy, Villejuif, France; [Institut Universitaire du Cancer - Oncopole, Toulouse, France](#); CHU Timone APHM, Aix-Marseille University, Marseille, France; CHRU Lille, Lille, France; Hospices Civils De Lyon, Cancer Research Center of Lyon, Claude Bernard University Lyon, Pierre Béninte, France; CHU Saint-André, Bordeaux, France; Gustave Roussy Comprehensive Cancer Center, Villejuif, France; Roche Pharmaceutical Laboratory, Boulogne-Billancourt, France

[Abstract Disclosures](#)

**Abstract:**

**Background:** Vismodegib is a Hedgehog Pathway inhibitor (HPI) indicated for treatment of inoperable locally advanced basal-cell carcinoma (laBCC). Previous studies showed an objective response (OR) rate of 67%, including 34% of complete response (CR). Discontinuation of vismodegib is very frequent, mostly due to intolerable side-effects. Long-term response and predictive factors of relapse after suspension of vismodegib have not yet been evaluated, but should play a crucial role in the management of laBCC patients. **Methods:** We conducted an observational retrospective study in 9 onco-dermatological French units. Medical charts of laBCC patients treated with vismodegib from March 2012 until June 2016 were reviewed and patients with CR who stopped treatment were selected. Relapse was diagnosed clinically and/or histologically. A survival analysis was conducted, and predictive factors, characterization and management of relapse were studied. **Results:** 119 laBCC patients achieved CR and stopped treatment. 21 were lost to follow-up and 6 died before relapse. Event-free survival median was 18.4 months (12.1 – 24.1) and cumulative incidence of relapse at 36 months was 59.04% (48.05 - 70.04), implying that more than 40% of patients do not relapse. Multiple BCC and BCC not localized on the head and neck were associated with a higher risk of relapse, independently of the existence of Gorlin syndrome (HR = 3.3 (IC95 = 1.6 - 6.7) and 2.01 (IC95 = 1.05 - 3.87) respectively). Total duration of treatment was not associated with relapse. 50% (n = 27) of patients who relapsed during follow-up were retreated with vismodegib, with an OR of 85.2% (n = 23). 42% (n = 24) were eligible to surgery only and other patients received local treatments. **Conclusions:** Long term responders after vismodegib treatment discontinuation are frequent independently of the time exposure to the drug before and after CR. Most patients who relapse are still responder to vismodegib rechallenge. Patients with multiple or laBCC not localized on the head and neck are more at risk of relapse after discontinuation. This study emphasizes the interest of treatment of laBCC with HPI.

## **Initial efficacy of anti-lymphocyte activation gene-3 (anti-LAG-3; BMS-986016) in combination with nivolumab (nivo) in pts with melanoma (MEL) previously treated with anti-PD-1/PD-L1 therapy.**

Sub-category:

[Advanced Disease](#)

Category:

Melanoma/Skin Cancers

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

9520

Poster Board Number:

Poster Discussion Session (Board #128)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 9520)

Author(s): Paolo Antonio Ascierto, Ignacio Melero, Shailender Bhatia, Petri Bono, Rachel E. Sanborn, Evan J. Lipson, Margaret K. Callahan, Thomas Gajewski, [Carlos A. Gomez-Roca](#), F. Stephen Hodi, Giuseppe Curigliano, Marta Nyakas, Matthias Preusser, Yoshinobu Koguchi, Matthew Maurer, Raphael Clynes, Priyam Mitra, Satyendra Suryawanshi, Eva Muñoz-Couselo; Istituto Nazionale Tumori "Fondazione G.Pascale"- IRCCS, Naples, Italy; Clinica Universidad de Navarra, Pamplona, Spain; University of Washington Seattle Cancer Care Alliance, Fred Hutchinson Cancer Center, Seattle, WA; Comprehensive Cancer Center, Helsinki University

Hospital, Helsinki, Finland; Robert W. Franz Cancer Research Center, Earle A. Chiles Research Institute, Providence Cancer Center, Portland, OR; Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD; Memorial Sloan Kettering Cancer Center, New York, NY; University of Chicago Medical Center, Chicago, IL; [Institut Universitaire du Cancer - Oncopole, Toulouse, France](#); Dana-Farber Cancer Institute, Boston, MA; Istituto Europeo di Oncologia, Milano, Italy; Oslo University Hospital, Oslo, Norway; Medical University of Vienna, Comprehensive Cancer Center, Vienna, Austria; Bristol-Myers Squibb, Princeton, NJ; Vall d'Hebron University Hospital Institute of Oncology (VHIO), Barcelona, Spain

#### **Abstract Disclosures**

##### **Abstract:**

**Background:** Signaling via LAG-3 and other T-cell inhibitory receptors (eg, PD-1) can lead to T-cell dysfunction and tumor immune escape. Simultaneous blockade of LAG-3 + PD-1 may synergistically restore T-cell activation and enhance antitumor immunity. In a phase 1/2a study, BMS-986016 (IgG4 mAb targeting LAG-3) ± nivo (IgG4 mAb targeting PD-1) demonstrated tolerability, peripheral T-cell activation, and preliminary clinical activity (NCT01968109; Lipson E, et al. *J Immunother Cancer*. 2016;4[s1]:173 [P232]). Here we describe preliminary efficacy of BMS-986016 + nivo in pts with MEL whose disease progressed on/after prior anti-PD-1/PD-L1 therapy, along with updated safety from all dose expansion pts. **Methods:** Pts with MEL must have had prior anti-PD-1/PD-L1 (± anti-CTLA-4 or BRAF/MEK inhibitors) and progressive disease (PD). Pts received BMS-986016 80 mg + nivo 240 mg IV Q2W. Primary objectives were safety and objective response rate (ORR; complete [CR] + partial [PR] response), disease control rate (DCR; CR + uCR + PR + uPR + stable disease [SD] > 12 wk), and duration of response (RECIST v1.1). **Results:** At data cutoff, 43 pts with MEL had been treated with BMS-986016 + nivo following PD on/after prior anti-PD-1/PD-L1 with known prior best responses of 1 CR, 9 PR, 12 SD, and 16 PD. Of the 43 pts, 30 (70%) also had prior anti-CTLA-4, 20 (47%) had ≥ 3 prior therapies, and 15 (35%) had *BRAF* mutations. In the 31 efficacy-evaluable pts to date, ORR was 16% (confirmed/unconfirmed) and DCR was 45% with benefit observed even in some pts refractory to prior anti-PD-1. Evaluations are ongoing for most pts, with median treatment duration of 10 wk for all 43 pts. Immunopathologic (eg, PD-1/PD-L1 and LAG-3 expression) and clinical characteristics of responders vs nonresponders will be presented. Any grade and grade 3/4 treatment-related AEs occurred in 46% and 9%, respectively, across all dose expansion pts (n = 129). **Conclusion:** Addition of BMS-986016 to nivolumab demonstrates encouraging initial efficacy in pts with MEL whose disease progressed on/after prior anti-PD-1/PD-L1 therapy, and a safety profile similar to nivolumab monotherapy. Clinical trial information: [NCT01968109](#)

## **Clinical utility of colon cancer molecular subtypes: Validation of two main colorectal molecular classifications on the PETACC-8 phase III trial cohort.**

Sub-category:

[Biomarkers/Epidemiology/Outcomes](#)

Category:

Gastrointestinal (Colorectal) Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

3509

Citation:

*J Clin Oncol* 35, 2017 (suppl; abstr 3509)

Author(s): Laetitia Marisa, Mira Ayadi, Ralyath Balogoun, Camilla Pilati, Karine Le Malicot, Come Lepage, Jean-François Emile, Ramon Salazar, Daniela Ellen Aust, Alex Duval, [Janick Selves](#), Dominique Esperance Guenet, Gerard A. Milano, Jean-François Seitz, Julien Taieb, Valerie Boige, Aurelien De Reynies, Pierre Laurent-Puig; Ligue Nationale Contre le Cancer, Paris, France; Université Paris Descartes, Sorbonne Paris Cité, France; Assistance Publique Hôpitaux de Paris, Department of Biology, Hôpital Européen Georges Pompidou, INSERM UMR-S1147, Paris, France; INSERM UMR-S 1147, Paris, France; FFCD, Dijon, France; CHU Le Bocage HGE, INSERM U866, Dijon, France; Versailles University and Hospital Ambroise Pare, AP-HP, Boulogne, France; Institut Català D'Oncologia, L'Hospitalet de Llobregat, Barcelona, Spain; University Hospital Carl Gustav Carus, Dresden, Germany; Sorbonne Universités, UPMC Univ Paris 06, INSERM, Centre de Recherche Saint-Antoine (CRSA), Paris, France; [INSERM U563, Toulouse, France](#); Strasbourg University, Strasbourg, France;

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#### [Abstract Disclosures](#)

#### Abstract:

**Background:** The molecular subtyping of colon cancers (CC) has been the subject of several recent publications, leading to an international consensus. The clinical relevance of these molecular classifications remains to be evaluated on large prospective patient cohorts using a tool that can be widely used on formalin-fixed paraffin-embedded (FFPE) samples. **Methods:** We aimed to evaluate the clinical relevance of two molecular subtyping systems, CMS (Guinney et al. 2015) and CCMST (Marisa et al. 2013), on the PETACC-8 cohort, a randomized phase III trial comparing adjuvant FOLFOX with or without cetuximab in patients with stage III CC. For each of these two classification systems, a predictor tool was developed and adapted to FFPE samples. The NanoString nCounter platform was used to screen 196 genes. Predictors were built from 249 frozen tumor samples previously used to build our classification system and 61 new paired FFPE/frozen samples. Both predictors were then applied to 1781 PETACC-8 FFPE samples. Subtypes associations to clinical and molecular features were analyzed. **Results:** The CMS predictor assigned 297 samples to CMS1 (17%), 585 to CMS2 (34%), 68 to CMS3 (4%) and 770 to CMS4 (45%). CMS were significantly associated with several molecular and clinical features, including MSI status (49% in CMS1,  $p < 0.001$ ), CIMP status (47% in CMS1,  $p < 0.001$ ), KRAS mutation (75% in CMS3,  $p < 0.001$ ), BRAF mutation (34% in CMS1,  $p < 0.001$ ), tumor location (less proximal tumors in CMS2,  $p < 0.001$ ), validating the predictor tool developed. The classification was significantly associated to prognosis in multivariate analysis, CMS4 subtype having a shorter overall survival (hazard ratio = 1.7,  $p = 0.021$ ). A deleterious effect of cetuximab was observed in CMS1 ( $p < 0.05$ ). Similar results were obtained with the CCMST classification. **Conclusions:** We validated molecular CC subtyping predictors for both CMS and CCMST classifications on PETACC-8 FFPE samples. The prognostic value of CMS and CCMST classifications was confirmed, stem-like tumors being associated with a poor prognosis. These results pave the avenue for widely use of the CC molecular classification in clinical routine.

## **Weekly paclitaxel (WP) +/- bevacizumab (B) in angiosarcoma (AS) patients (pts): Analysis of prognostic/predictive factors from a randomized phase 2 trial.**

Sub-category:

[Bone Tumors](#)

Category:

Sarcoma

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

11024

Poster Board Number:

Poster Session (Board #347)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 11024)

Author(s): Loic Lebellec, Francois Bertucci, Emmanuelle Tresch-Bruneel, Isabelle Laure Ray-Coquard, Axel Le Cesne, Emmanuelle Bompas, Sophie Piperno-Neumann, Antoine Italiano, [Christine Chevreau](#), Didier Cupissol, Jacques-Olivier Bay, Olivier Collard, Esma Saada-Bouزيد, Nicolas Isambert, Corinne Delcambre, Jean-Yves Blay, Anthony Goncalves, Nicolas Penel; Centre Oscar Lambret, Lille, France; Institut Paoli-Calmettes, Marseille, France; Centre Léon-Bérard, Lyon, France; Gustave Roussy Cancer Campus, Villejuif, France; Centre René Gauducheau, Nantes, France; Medical Oncology, Institut Curie, Paris, France; Institut Bergonié, Bordeaux, France; [IUCT-Oncopôle /Institut Claudius Regaud, Toulouse, France](#); Institut de Cancérologie de Montpellier, Montpellier, France; Cellular Therapy and Clinic Hematology Unit for Adults, Clermont-Ferrand, France; Institut de Cancérologie de la Loire, St. Priest en Jarez, France; Centre Antoine

Lacassagne, Nice, France; Centre Georges-François Leclerc, Dijon, France; Centre François Baclesse, Caen, France; Department of Medical Oncology, Institut Paoli-Calmettes, Marseille, France

#### Abstract Disclosures

Abstract:

**Background:** WP is an active regimen for treatment of AS pts (Ray-Coquard JCO 2015). We report here the correlative analysis conducted during a phase 2 trial assessing WP +/- B. **Methods:** Circulating pro/anti-angiogenic factors (FGF, PIGF, SCF, Selectin, thrombospondin, VEGF, VEGF-C) were collected at D1 and D8. Prognostic value for PFS was assessed using Cox model (biomarkers as continuous variables). We attempt to identify subgroups of pts benefiting from adding B using interaction tests (predictive factors). **Results:** Among the 51 pts enrolled in this trial, 45 were analyzable: 20 in Arm A (WP without B) and 25 in Arm B (with B). Median PFS was 5.5 and 6.1 months, respectively ( $p = 0.84$ ). Samples were collected in 45 pts at D1 and 42 pts at D1 and 8. Baseline biomarkers were similar in both arms (excluding Selectin, significantly lower in arm A: median of 25 vs. 35 ng/mL,  $p = 0.03$ ). In arm A, there was no significant difference between values at D1 and D8. In arm B, there were a significant decrease in VEGF (from a median of 0.49 to 0.08 ng/mL;  $p < 0.01$ ) and selectin (from a median of 35.3 to 31.7 ng/mL;  $p < 0.01$ ), and a significant increase in PIGF (from a median of 16.1 to 30.0 pg/mL;  $p < 0.01$ ). In univariate analysis, factors associated with PFS were: de novo vs. radiation-induced AS (HR = 2.39 ( $p < 0.01$ ), visceral vs. superficial AS (HR = 2.04;  $p < 0.03$ ), VEGF-C at D1 (HR = 0.77;  $p < 0.03$ ), FGF at D8 (HR = 1.17;  $p < 0.01$ ), difference in FGF D8-D1 (HR = 1.24;  $p < 0.01$ ), and PIGF value at D1 (HR = 1.02;  $p < 0.05$ ). In multivariate analysis, factors associated with PFS were: de novo AS (HR = 2.39;  $p = 0.03$ ), VEGF-C at D1 (HR = 0.73;  $p < 0.02$ ) and FGF difference between D8 and D1 (HR = 1.16;  $p < 0.02$ ). None of these factors were associated with benefit of adding B. **Conclusions:** Baseline VEGF-C levels and change in FGF were independent prognostic factors in pts with or without B. Addition of B significantly decreased the level of circulating VEGF and selectin and increased the level of circulating PIGF in AS patients. We did not identify subgroup of pts benefiting from adding of B to WP. Clinical trial information: [NCT01303497](#)

## Pharmacogenomic determinants of cetuximab and oxaliplatin pharmacokinetics during combined intravenous cetuximab (IV-Cet) and triplet hepatic artery chronomodulated infusion in patients (pts) with initially unresectable liver metastases from colorectal cancer (uLM-CRC) (EU OPTILIV trial).

Sub-category:

[Pharmacology](#)

Category:

Developmental Therapeutics—Clinical Pharmacology and Experimental Therapeutics

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

e14082

Citation:

J Clin Oncol 35, 2017 (suppl; abstr e14082)

Author(s): Abdoulaye Karaboue, Raphael Saffroy, Christophe Desterke, Mohamed Bouchahda, Pasquale Innominato, C. N. J. Focan, [Etienne Chatelut](#), Gilles Paintaud, Gerard A. Milano, Antoinette Lemoine, Francis Levi; AK-SCIENCE, Vitry Sur Seine, France; Hopital Paul Brousse Biochemistry Department, University Paris-Sud, Villejuif, France; Universite Paris Sud 11 UMS33 INSERM Unit, Villejuif, France; Paul Brousse Hospital, Oncology Department, Villejuif, French Southern Territories; University of Warwick, Medical School, Coventry, United Kingdom; Department of Oncology, Centre Hospitalier Chrétien, Clinique Saint-Joseph, Liege, Belgium; [Institut Claudius Regaud, IUCT-Oncopole, CRCT, Inserm, Toulouse, France](#); Universite François-Rabelais de Tours, CNRS, GICC UMR 7292, CHRU de Tours, Service de Pharmacologie-Toxicologie, Tours, France; Oncopharmacology Unit, Centre Antoine Lacassagne, Nice, France; Paul Brousse Hospital, Villejuif, France; Warwick University, Coventry, United Kingdom

#### Abstract Disclosures

Abstract:

**Background:** Triplet HAI with IV-Cet achieved 29.7% complete uLM-CRC resections (R0+R1) and an overall median survival (OS) of 25.7 months in previously treated pts. While the high antitumour efficacy of this new regimen involved direct exposure of LM to the HAI drugs and their potentiation by cetuximab, haematological and intestinal toxicities mostly related to systemic exposure (Lévi, Ann Oncol 2016; Clin Pharmacokin 2016). **Methods:** To identify potential pharmacogenomics (PG) determinants of toxicity-related systemic exposure to the HAI drugs, 207 single nucleotide polymorphisms (SNPs) from 34 pharmacology genes were analysed in blood mononuclear cells (ADME PGx, MassArray platform, Sequenom, USA) from 11 pts undergoing a first course of chronomodulated triplet HAI and iv-CET (Levi et al. Clin Pharmacokin 2016). Relations between SNPs and main pharmacokinetics parameters and toxicities were determined using ANOVA or Fisher Exact test. **Results:** Nine toxicity-related polymorphic genes were identified in the 52 pts of the PG study (ASCO, submitted). Here we investigated whether any of these polymorphic genes modified PK in 4F and 7M (33-72 yo) with WHO performance status 0-1. ABCB1 (rs1045642) was the only polymorphic gene that was significantly associated with both pharmacokinetics and toxicity in this study population. **Conclusions:** ABCB1 polymorphisms

might contribute to the systemic hematologic toxicity of the combined IV-HAI regimen through altering cetuximab and oxaliplatin disposition, yet without affecting efficacy. Consideration of ABCB1 polymorphism could help optimize OPTILIV delivery in individual patients. Clinical trial information: [NCT00852228](https://clinicaltrials.gov/ct2/show/study/NCT00852228)

Gene (accession number)	PG population (N=52) Genotype	Neutropenia Grade 3-4	Oxaliplatin (N=11)	Cetuximab (N=11)	
			Cmax [ng/mL] Mean ± SEM	Cmax [ng/mL] Mean ± SEM	AUC [ng*mn/mL] Mean ± SEM
ABCB1 rs 1045642	C/T	41.9%	1012 ± 74	318 ± 33	266,948 ± 15,763
	C/C	10.0%	673 ± 94	243 ± 32	227,916 ± 26,291
	T/T	75.0%	1075 ± 25	445 ± 35	395,341 ± 38,069
<i>P</i>		0.015 <sup>a</sup>	0.0328 <sup>b</sup>	0.0164 <sup>b</sup>	0.005 <sup>b</sup>

<sup>a</sup>Fisher exact; <sup>b</sup>ANOVA.

## Post-cross-over activity of regorafenib (RE) in soft tissue sarcoma: Analysis from the REGOSARC trial.

Sub-category:

[Soft Tissue](#)

Category:

Sarcoma

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

11052

Poster Board Number:

Poster Session (Board #375)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 11052)

Author(s): Nuria Kotecki, Thomas Brodowicz, Axel Le Cesne, Marie-Cecile Le Deley, Jennifer Wallet, Antoine Italiano, Jean-Yves Blay, Francois Bertucci, [Christine Chevreau](#), Sophie Piperno-Neumann, Emmanuelle Bompas, S Bastien Salas, Christophe Perrin, Corinne Delcambre, Bernadette Lieg-Atzwanger, Maud Toulmonde, Isabelle Laure Ray-Coquard, Julien Thery, Olivier Mir, Nicolas Penel; Oscar Lambret Center, Lille, France; Medical University of Vienna, Vienna, Austria; Gustave Roussy Cancer Campus, Villejuif, France; Centre Oscar Lambret, Lille, France; Institut Bergonié, Bordeaux, France; Centre Léon-Bérard, Lyon, France; Institut Paoli-Calmettes, Marseille, France; [IUCT-Oncopôle /Institut Claudius Regaud, Toulouse, France](#); Medical Oncology, Institut Curie, Paris, France; Centre René Gauducheau, Nantes, France; Hopital de la Timone, Marseille, France; Centre Eugène Marquis, Rennes, France; Centre François Baclesse, Caen, France; Graz Medical University, Graz, Austria; Institut Bergonié, Department of Medical Oncology, Bordeaux, France; Gustave Roussy, Villejuif, France

### Abstract Disclosures

Abstract:

**Background:** Based on the placebo (PBO) controlled phase 2 trial (Mir, Lancet Oncol 2016), RE has shown to be an active drug in patients (pts) with leiomyosarcoma (LMS), synovial sarcoma (SS) and other non-adipocytic sarcoma (OTH), but not in liposarcoma. Pts initially allocated to PBO were allowed to cross-over to RE after progression. We here report the activity of RE after cross-over. **Methods:** From July 2013 to Dec 2014, 138 pts were enrolled in the non-adipocytic sarcoma cohorts (LMS, SS & OTH). After update in Dec 2016, median follow-up was 32 mo (vs 17 mo in the initial publication). Benefit of RE vs PBO in terms of progression-free survival (PFS) and overall survival (OS) from randomization was estimated by hazard ratio (HR) in Cox models. In the PBO arm, intra-patient benefit of RE after cross-over was evaluated by the growth modulation index (GMI), where PFS1=PFS with PBO before cross-over, and PFS2=PFS with RE after cross-over. The impact of timing of RE allocation (delayed after cross-over, vs early at study entry) was evaluated by comparing PFS after cross-over in PBO arm to PFS after randomization in RE arm. **Results:** As detailed in the table, major PFS benefit of RE vs PBO allocated by randomization was confirmed with long follow-up (HR=0.50 [95%CI 0.35-0.71] p<.0001). However, this translates into a smaller and non-significant OS benefit (HR=0.78 [0.54-1.12] p=.18). This finding may partially be explained by the fact that 55 of the 68 pts who progressed in the PBO arm (81%) could receive RE after progression and benefit from RE: 56% of them had a GMI greater than 1.3. Delayed start of RE was associated with a non-significantly shorter PFS compared to earlier treatment (HR=1.21, [0.84-1.73] p=.30). **Conclusions:** Efficacy of RE vs PBO is confirmed with longer

follow-up in non-adipocytic sarcoma. PFS of pts receiving RE after cross-over is not significantly shorter than that of pts initially randomized to receive RE. Clinical trial information: [NCT01900743](https://clinicaltrials.gov/ct2/show/study/NCT01900743)

	RE at randomization		PBO at randomization		RE post cross-over (PBO arm)		RE vs PBO post-randomization		Delayed vs early RE	
	N	PFS (mo)	N	PFS1 (mo)	N	PFS2 (mo)	HR	p	HR	p
<b>LMS</b>	28	3.7	28	1.8	22	2.6	0.60	.059	1.35	.31
<b>SS</b>	13	3.8	14	1.0	13	2.0	0.09	<.0001	1.45	.36
<b>OTH</b>	28	2.9	27	1.0	20	2.8	0.57	.04	1.00	.99
<b>All</b>	69	3.7	69	1.0	55	2.6	0.50	<.0001	1.21	.30

## COMBI-MB: A phase II study of combination dabrafenib (D) and trametinib (T) in patients (pts) with *BRAF* V600–mutant (mut) melanoma brain metastases (MBM).

Sub-category:

[Advanced Disease](#)

Category:

Melanoma/Skin Cancers

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

9506

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 9506)

Author(s): Michael A. Davies, Caroline Robert, Georgina V. Long, Jean Jacques Grob, Keith T. Flaherty, Ana Arance, Vanna Chiarion-Sileni, Luc Thomas, Thierry Lesimple, Laurent Mortier, Stergios J. Moschos, David Hogg, Ivan Marquez Rodas, Michele Del Vecchio, Celeste Lebbe, [Nicolas Meyer](#), Ying Zhang, Yingjie Huang, Bijoyesh Mookerjee, Philippe Saiag; The University of Texas MD Anderson Cancer Center, Houston, TX; Gustave Roussy Comprehensive Cancer Center, Villejuif, France; Melanoma Institute of Australia and The University of Sydney, Sydney, Australia; Aix-Marseille University, Marseille, France; Dana-Farber Cancer Institute/Harvard Medical School and Massachusetts General Hospital, Boston, MA; Hospital Clínic de Barcelona, Barcelona, Spain; Veneto Oncology Research Institute, Padua, Italy; Centre Hospitalier Lyon-Sud, Lyon, France; Centre Eugène Marquis, Rennes, France; Centre Hospitalier Universitaire Lille, Lille, France; University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC; Princess Margaret Cancer Centre, Toronto, ON, Canada; Hospital General Universitario Gregorio Marañón, Madrid, Spain; [Fondazione IRCCS Istituto Nazionale dei Tumori](#), Milan, Italy; University Paris Diderot, Paris, France; [Institut Universitaire du Cancer - Oncopole, Toulouse, France](#); Novartis Pharmaceuticals Corporation, East Hanover, NJ; Université Versailles Saint-Quentin-en-Yvelines, Versailles, France

[Abstract Disclosures](#)

Abstract:

**Background:** CNS metastases are common and associated with very poor prognosis in pts with metastatic melanoma (MM). In the phase II BREAK-MB trial, D had clinical activity in *BRAF* V600–mut MBM. D + T has shown superiority over D alone in pts with *BRAF* V600–mut mm without MBM; however, efficacy of this regimen on MBM has not been characterized. Here, we report results from a phase II trial of D + T in *BRAF*V600–mut MBM (COMBI-MB; NCT02039947). **Methods:** This open-label, phase II study evaluated D 150 mg BID + T 2 mg QD in 4 MBM cohorts: (A) *BRAF*V600E, asymptomatic MBM, no prior local treatment (Tx); (B) *BRAF*V600E, asymptomatic MBM, prior local Tx; (C) *BRAF*V600D/K/R, asymptomatic MBM, with or without prior local Tx; and (D) *BRAF*V600D/E/K/R, symptomatic MBM, with or without prior local Tx. The primary objective was intracranial response rate (IRR) in cohort A (null hypothesis, IRR ≤ 35%). Secondary endpoints included IRR in cohorts B, C, and D; extracranial (ERR) and overall (ORR) response rates; intracranial (IDCR), extracranial (EDCR), and overall (ODCR) disease control rates; duration of IR, ER, and OR; PFS; OS; and safety. **Results:** 125 pts were enrolled (A, n = 76; B, n = 16; C, n = 16; D, n = 17). In cohort A, median age was 52, 53% were male, and 37% had LDH > ULN. At data cutoff (28 Nov 2016; median f/u, 9.0 mo), in cohort A, investigator-assessed IRR was 58% (IDCR, 78%), ERR was 55% (EDCR, 80%), and ORR was 58% (ODCR, 80%). Median duration of IR, ER, and OR was 6.5 mo (95% CI, 4.9-10.3), 10.2 mo (95% CI, 6.5-13.0), and 6.5 mo (95% CI, 4.9-10.3), respectively. Median PFS was 5.6 mo (95% CI, 5.3-7.4). Independent review supported these results. 6-mo OS was 79%; with 31 pts (41%) still in f/u, preliminary median OS was 10.8 mo (95% CI, 8.7-19.6). Efficacy in cohorts B, C, and D



will be reported. AEs across cohorts (any, 98%; grade 3/4, 48%) were consistent with prior D + T studies; 10% of pts (8% in cohort A) discontinued due to AEs. **Conclusions:** In this first report of a phase II trial evaluating a BRAF and MEK inhibitor combination in *BRAF*V600-mut MBM, the primary endpoint was met. Promising IRR and IDCR were seen with D + T, but responses appear less durable than reported for mm without MBMs. No unexpected safety issues were observed. Clinical trial information: [NCT02039947](#)

## Randomized controlled phase III study evaluating the impact of secondary cytoreductive surgery in recurrent ovarian cancer: AGO DESKTOP III/ENGOT ov20.

Sub-category:

[Ovarian Cancer](#)

Category:

Gynecologic Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

5501

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 5501)

Author(s): Andreas Du Bois, Ignace Vergote, [Gwenael Ferron](#), Alexander Reuss, Werner Meier, Stefano Greggi, Pernille Tina Jensen, Frédéric Selle, Frederic Guyon, Christophe Pomel, Fabrice Lecuru, Rongyu Zang, Elisabeth Avall-Lundqvist, Jae Weon Kim, Jordi Ponce, Francesco Raspagliesi, Sadaf Ghaem-Maghani, Alexander Reinthaller, Philipp Harter, Jalid Sehoul; AGO and Kliniken Essen Mitte, Essen, Germany; BGOG and University of Leuven, Leuven Cancer Institute, Leuven, Belgium; [GINECO and Institut Claudius Regaud, Toulouse, France](#); AGO and Coordinating Center for Clinical Trials, Marburg, Germany; AGO and Frauenklinik, Evangelisches Krankenhaus Duesseldorf, Duesseldorf, Germany; MITO and Istituto Nazionale Dei Tumori, Naples, Italy; NSGO and Odense University Hospital, Odense, Denmark; GINECO and Hôpital Tenon, Paris, France; GINECO and Institut Bergonié, Bordeaux, France; GINECO and Centre Jean Perrin, Clermont-Ferrand, France; GINECO and European Georges Pompidou Hospital, Paris, France; SGOG and Shanghai Fudan University, Shanghai, China; NSGO and Linköping University and Karolinska Institute, Linköping, Sweden; KGOG and Seoul National University, Seoul, Korea South; GEICO and Bellvitge Hospital, Barcelona, Spain; MITO and Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy; NCRI and Imperial College London, London, United Kingdom; AGO-Austria and University of Vienna, Vienna, Austria; AGO and Charité Campus Virchow-Klinikum, Berlin, Germany

### [Abstract Disclosures](#)

Abstract:

**Background:** The role of secondary cytoreductive surgery in recurrent ovarian cancer (OC) has not been defined by level-1 evidence. **Methods:** Pts with OC and 1st relapse after 6+ mos platin-free interval (TFIp) were eligible if they presented with a positive AGO-score (PS ECOG 0, ascites ≤500 ml, and complete resection at initial surgery) and were randomized to 2<sup>nd</sup>-line chemotherapy alone vs cytoreductive surgery followed by chemo. Chemo regimens were selected according to the institutional standard. We report here results of the predetermined interim analysis. **Results:** 407pts were randomized 2010-2014. The TFIp exceeded 12 mos in 75% and 76% pts in both arms. 8.9% of 203 pts were operated despite of randomization to the no-surgery arm, whereas 6.9% of 204 pts in the surgery arm did not undergo operation. Complete resection was achieved in 67% of pts; 87% and 88% received a platinum-containing 2<sup>nd</sup>-line therapy. Median PFS was 14 mos without and 19.6 mos with surgery (HR: 0.66, 95%CI 0.52-0.83, p<0.001). Median time to start of first subsequent therapy (TFST) was 21 vs 13.9 mos in favor of the surgery arm (HR 0.61, 95%CI 0.48-0.77, p=p<0.001). PFS-2 between 1<sup>st</sup> and 2nd relapse equaled or even exceeded PFS-1 before 1<sup>st</sup>relapse in 26% after surgery and only 16% without-surgery. Analysis of the primary endpoint OS is kept blinded due to immaturity and will be evaluated after extended follow-up (the observed pooled unblinded 2-YSR was 83% instead of the initially in the protocol assumed 55-66%). 60d mortality rates were 0 and 0.5% in the surgery and no-surgery arm. Re-laparotomies were performed in 7 pts (3.5%) in the surgery arm. With the exception of myelosuppression which occurred more frequently in the no-surgery arm no further significant differences were observed with respect to grade 3+ acute adverse events. **Conclusions:** Surgery in pts with 1st relapse of OC after a TFIp of 6+ mos and selected by a positive AGO-Score resulted in a clinically meaningful increase of PFS and TFST with acceptable treatment burden. Until final OS data will definitively define the role of secondary cytoreductive surgery it should at least be considered as valuable option in pts with a positive AGO-Score. Clinical trial information: [NCT01166737](#)

## Efficacy and safety of nivolumab in patients with metastatic renal cell carcinoma (mRCC) and brain metastases: Preliminary results from the GETUG-AFU 26 (Nivoren) study.

Sub-category:

[Kidney Cancer](#)

Category:

Genitourinary (Nonprostate) Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

4563

Poster Board Number:

Poster Session (Board #241)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 4563)

Author(s): Bernard J. Escudier, Sylvie Chabaud, Delphine Borchellini, Gwenaëlle Gravis, [Christine Chevreau](#), Pierre Emmanuel Brachet, Lionnel Geoffrois, Brigitte Laguerre, Hakim Mahammed, Sylvie Negrier, Frederic Rolland, Marine Gross Goupil, Muriel Habibian, Laurence Albiges; Gustave Roussy Cancer Campus, Villejuif, France; Centre Léon-Bérard, Lyon, France; Department of Medical Oncology, Centre Antoine-Lacassagne, Nice, France; Institut Paoli-Calmettes, Marseille, France; [IUCT-Oncopôle /Institut Claudius Regaud, Toulouse, France](#); Centre François Baclesse, Caen, France; Department of Medical Oncology, Institut de Cancérologie de Lorraine, Vandœuvre-Lès-Nancy, France; Centre Eugène Marquis, Rennes, France; Centre Jean Perrin, Clermont-Ferrand, France; Department of Medical Oncology, Institut de Cancérologie de l'Ouest, Nantes, France; CHU Bordeaux, Bordeaux, France; Unicancer, Paris, France; Gustave Roussy Cancer Campus and University Paris-Sud, Villejuif, France

[Abstract Disclosures](#)

**Abstract:**

**Background:** Nivolumab (N) has been shown active in patients (pts) with mRCC after failure of 1 or 2 TKIs.

Efficacy and safety of N in pts with brain metastases (BM) from RCC is still unknown. The aim of this study is to report preliminary data of the Nivoren study in pts with BM. **Methods:** GETUG-AFU 26 (Nivoren) is a prospective phase 2 study assessing safety and efficacy of N in a broader mRCC patient population than those recruited in the pivotal phase 3, including pts with BM (previously treated or not, but not requiring steroids), with previous mTOR inhibitor, with PS 2 as well as in previously highly pretreated pts. N was given every 2 weeks at 3mg/kg, until disease progression or unacceptable toxicity. Treatment was allowed beyond progression in case of clinical benefit. All pts had brain CT scan or MRI at baseline. **Results:** Up to December 2016, 588 pts have been enrolled including 55 pts with BM (35 (67%), 6 (12%) and 11 (21%) with 1, 2 or > 2 BM, respectively. Of those 55 pts, 10 pts (23%) were PS 2 and 25 (58%) PS 1, and 16 patients (29%) had received more than 2 lines of therapy. No previous treatment for BM was performed in 67% (n = 37), while 9% had previous brain surgery (n = 5) or brain radiation (n = 17 (31%)). 2/55 pts never received N. Median duration of therapy in BM pts was 2.4 months (varying from 0 to 9) with a 3-months PFS of 60% (IC95% = 45 – 73). Median OS is not reached at the time of this analysis. Among 44 pts with assessment of response on BM, 10 (23%) had objective response while 21 (48%) had local progressive disease. Neurologic deterioration requiring steroids was observed in 15 pts (32%). Updated data will be presented at the meeting. **Conclusions:** This is the first large study to report preliminary safety and efficacy of N in RCC pts with BM. Safety of N in this pt population appears to be acceptable, although some pts do require steroids because of brain progressive disease. Objective response in the brain was observed in 23% of pts. Further follow up is required to determine the real benefit of N in this group of mRCC pts. Clinical trial information: [NCT03013335](#)

### **Outcome of 212 malignant phyllod tumor patients: A retrospective study from the French Sarcoma Group (GSF-GETO).**

Sub-category:

[Soft Tissue](#)

Category:

Sarcoma

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

11055

Poster Board Number:

Poster Session (Board #378)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 11055)

Author(s): Mathias Neron, Christophe Sajous, Sophie Piperno Neumann, Camille Chakiba, Agnes Ducoulombier, Clémentine Owen, S Bastien Salas, Francois Bertucci, Esma Saada-Bouزيد, [Thibaud Valentin](#), Jacques-Olivier Bay, Emmanuelle Bompas, Nicolas Isambert, Aurélie Maran-Gonzalez, Carmen Llacer, Sebastien Carrère, Didier Cupissol, Simon Thezenas, Jean-Yves Blay, Nelly Firmin, French Sarcoma Group (GSF-GETO); Institut du Cancer de Montpellier, Montpellier, France; Centre Léon-Bérard, Lyon, France; Institut Curie, Paris, France; Institut Bergonié, Bordeaux, France; Centre Oscar Lambret, Lille, France; Institut Gustave Roussy, Villejuif, France; Hopital de la Timone, Marseille, France; Institut Paoli-Calmettes, Marseille, France; Centre Antoine Lacassagne, Nice, [France; Oncopole, Toulouse, France](#); Centre

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### Abstract Disclosures

#### Abstract:

**Background:** The optimal management of malignant phyllod tumors (MPT) is poorly documented. Objective: To study the characteristics and outcome of MPT patients (pts). **Methods:** Retrospective study from the nation-wide French sarcoma network (NetSarc) from 2000 to 2016. Inclusion criteria was central pathological review of MPT. End-points were local recurrence-free survival (LRFS), metastasis-free survival (MFS), and overall survival (OS). **Results:** 212 pts, from 13 centers, were included. Median age was 52.8 years (range: 16.8 - 90.5). All localized MPT pts (96.7%) underwent surgery with 41.4% of mastectomy. The median size was 5.8 cm (range: 1.5 - 30). R1/R2 resection was achieved in 40.1% pts (26.9% 1-2 mm margin, 12.2% 3-7 mm, 20.3%  $\geq 8$  mm), with 44.8% of second surgery (SS) for a final mastectomy rate of 72.6%. Presurgical biopsy was performed in 86.3% and associated with R0 resection ( $p=0.044$ ) and better LRFS ( $p=0.012$ ). Median follow-up was 4.1 years (range 0-14.8) and revealed 34 (16.6%), 48 (22.9%), 44 (20.8%) events for LRFS, MFS and OS, respectively. The 2-year OS rate was 89%. Prognostic factors found in multivariate analysis are presented in Table 1. Wider margins ( $\geq 8$ mm) were not associated with better outcomes. Adjuvant radiotherapy and chemotherapy were performed in 43.6% and 13.3% respectively and associated with longer LRFS, not significant in multivariate analysis. **Conclusions:** Mastectomy is associated with better local control, but not with MFS and OS. Age, tumor necrosis and metastatic disease are associated with poor prognosis in MPT pts. Our study suggests that margins of 3 mm are necessary and sufficient for the surgical management of MPT and emphasizes the importance of SS to obtain clear margins.

End Point	Variable	Hazard Ratio	p
		Yes	1
	<b>Mastectomy at first or SS</b>	No	4,85
		0-2 without SS	1
		0-2 with SS	0,82
<b>LRFS</b>	<b>Margins (mm)</b>	$\geq 3$	0,68
	<b>Age (y)</b>	<50	1
		$\geq 50$	2,14
	<b>Tumor necrosis</b>	Yes	1,96
		No	1
		0-2 without SS	1
		0-2 with SS	0,3
<b>MFS</b>	<b>Margins (mm)</b>	$\geq 3$	0,75
		Yes	5,27
	<b>Metastatic disease at diagnosis</b>	No	1
	<b>Metastatic recurrence</b>	Yes	7,29
		No	1
		0-2 without SS	1
		0-2 with SS	0,32
<b>OS</b>	<b>Margins (mm)</b>	$\geq 3$	0,55

Prognostic factors for each end-point (multivariate analysis).

## Combination of pembrolizumab and metronomic cyclophosphamide in patients with advanced sarcomas and GIST: A French Sarcoma Group phase II trial.

Sub-category:

Soft Tissue

Category:

Sarcoma

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

11053

Poster Board Number:

Poster Session (Board #376)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 11053)

Author(s): Maud Toulmonde, Nicolas Penel, Julien Adam, [Christine Chevreau](#), Jean-Yves Blay, Axel Le Cesne, Emmanuelle Bompas, Sophie Piperno-Neumann, Sophie Cousin, Thomas Rycckewaert, Alban Bessede, Francois Ghiringhelli, Thomas Grellety, Marina Pulido, Antoine Italiano; Institut Bergonié, Department of Medical Oncology, Bordeaux, France; Centre Oscar Lambret, Lille, France; Gustave Roussy, Drug Development Department (DITEP); Inserm U981, Villejuif, France; [IUCT-Oncopôle /Institut Claudius Regaud, Toulouse, France](#); Centre Léon-Bérard, Lyon, France; Gustave Roussy Cancer Campus, Villejuif, France; Centre René Gauducheau, Nantes, France; Medical Oncology, Institut Curie, Paris, France; Institut Bergonié, Bordeaux, France; ImmuSmol, Pessac, France; Centre Georges-François Leclerc, Dijon, France; Department of Medical Oncology - Institut Bergonié, Bordeaux, France

#### [Abstract Disclosures](#)

Abstract:

**Background:** There is a good rationale for immunotherapy in sarcoma. We report results of the first open-label multicentre phase 2 study assessing the anti-PD-1 antibody pembrolizumab in combination with metronomic cyclophosphamide (CP) in patients (pts) with advanced soft tissue sarcomas (STS) and gastro-intestinal stromal tumor (GIST). **Methods:** This trial included 4 cohorts of pts with advanced STS: leiomyosarcoma (LMS), undifferentiated pleomorphic sarcoma (UPS), other sarcomas (Others), and GIST. All pts received CP 50 mg BID one week on, one week off, and pembrolizumab 200mg IV q21 days. The primary endpoint encompassed non-progression and objective response at 6 months per RECIST evaluation criteria v1.1 for LMS, UPS, and Others, and 6-month non-progression for GIST. Correlative studies of immune biomarkers were planned on pt's tumor and plasma samples. **Results:** Between June 2015 and July 2016, 57 pts were included, and 50 were assessable for efficacy. Three pts experienced tumor shrinkage resulting in a partial response (PR) in one of them. The 6-month non-progression rate was 0%, 0%, 14.3% (95%CI 1.8-42.8), and 11.1% (95%CI 2.8-48.3) in LMS, UPS, Others, and GIST respectively. The most frequent adverse events were grade 1 or 2 fatigue, diarrhea, anemia. The only pt who experienced PR was the only one with a PD-L1-positive staining in more than 10% of immune cells on archived tumor sample. A strong macrophage infiltration was observed in tumor samples, and these macrophages largely expressed the inhibitory enzyme Indoleamine-2,3-dioxygenase-1 (IDO1). Moreover, a significant increase of the kynurenine/tryptophane ratio was observed in pts plasma samples during study treatment (p =0.0007). **Conclusions:** PD-1 inhibition has limited activity in advanced STS and GIST. This primary resistance may be explained by the low percent of PD-L1 positivity in these tumors, and an immune-suppressive tumor microenvironment resulting from macrophage infiltration and IDO1 pathway activation. Further strategies assessing drugs such as CSF1-R inhibitors and/or IDO inhibitors combined with anti-PD-1/PD-L1 in selected sarcoma subtypes are warranted. Clinical trial information: [NCT02406781](#)

## Characteristics of very long responder to maintenance cetuximab after a platinum-cetuximab based chemotherapy for recurrent and/or metastatic head and neck squamous cell carcinomas (RM HNSCC).

Sub-category:

[Biomarkers/Epidemiology/Outcomes](#)

Category:

Head and Neck Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

e17524

Citation:

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Author(s): Magalie Pascale Tardy, Celine Lescure, Jerome Doyen, Amaury Daste, Martin Lange, Mathilde Saint-Ghislain, Gautier Lefebvre, Victor Sarradin, Alexandre Bozec, Esma Saada-Bouzid, [Frederic Peyrade](#), Antoine Lacassagne Center, Nice, France; Eugène Marquis Center, Rennes Cedex, France; Centre Antoine Lacassagne, Nice, France; Hôpital Saint André, CHU de Bordeaux, Bordeaux, France; Centre Hospitalier Lyon-Nord, Lyon, France; Institut Curie, Paris, France; Centre Oscar Lambret, Lille, France; [Oncopole, Toulouse, France](#)

#### [Abstract Disclosures](#)

Abstract:

**Background:** Standard treatment for first line RM HNSCC is the association of platinum-5FU and cetuximab. For non-progressive patients (pts), cetuximab is given weekly as maintenance until progression or unacceptable toxicity. In the EXTREME protocol (Vermorken et al, NEJM 2008), this strategy showed an OS of 10.1 months with a mean duration of maintenance of 3 months. This study aimed at describing pts who have benefited from a cetuximab maintenance for a longer period (i.e. > 6 months). **Methods:** We did a retrospective study in 7 centers in France. Inclusion criteria were: pts > 18 years with a RM HNSCC treated between November 2009 and

January 2017, with platinum based chemotherapy and cetuximab followed by weekly cetuximab maintenance of more than 6 months. **Results:** 53 pts (45 male), with a median age of 57 [38-76] were recorded. Median follow-up was 63.7 months [14.8-237.6]. 72% [37/53] had an oral cavity or oropharynx tumor location with a well or moderately differentiated carcinoma (74%). 45/53 (85%) were smokers and 4/21 (19%) p16 positive. 46/53 (87%) had a Performans Status of 0-1. Mean BMI and albumin level were respectively 22.5 [SD: 4.19] and 40g/l [SD: 4.9]. EXTREME regimen was used for 44 pts, 2 pts had platinum and cetuximab and 7 received platinum, docetaxel and cetuximab. Mean number of chemotherapy cycles was 5 [3-7]. After chemotherapy, the number of pts with complete response (CR), partial response (PR) or stabilization was respectively 5 (9%), 23 (43%) and 25 (47%). 2 pts in PR finally achieved CR during maintenance. One of them stopped cetuximab and was still in CR 5 months later. Mean duration time of maintenance by cetuximab was 11 months [6-24]. Toxicities were mainly cutaneous: 47/53 pts had toxicities, of which 6 had grade 3. Presence of cutaneous toxicities seemed to be correlated with a longer response (p = 0.01). PFS and OS were respectively 15.5 and 27.4 months. **Conclusions:** Our study allowed us to identify a cohort of long responder pts to maintenance cetuximab including 2 pts who obtained a complete response. More analysis should be done to identify biomarkers able to predict long responder.

## TRUST: Trial of radical upfront surgical therapy in advanced ovarian cancer (ENGOT ov33 / AGO-OVAR OP7).

Sub-category:

[Ovarian Cancer](#)

Category:

Gynecologic Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

TPS5602

Poster Board Number:

Poster Session (Board #423a)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr TPS5602)

Author(s): Sven Mahner, Florian Heitz, Alexander Burges, Alexander Reuss, Bernhard Kraemer, Barbara Schmalfeldt, Jalid Sehouli, Bjoern Lampe, Andreas Schnelzer, Pauline Wimberger, Christina Fotopoulou, Frederic Guyon, Fabrice Lecuru, [Denis Querleu](#), Stefano Greggi, Nicoletta Colombo, Giovanni Damiano Aletti, Philipp Harter, Andreas Du Bois; Department for Gynecology and Obstetrics, University of Munich, Munich, Germany; Department of Gynecologic Oncology, Kliniken Essen-Mitte, Essen, Germany; AGO and Department of Gynecology, University Hospital Munich-Großhadern, Munich, Germany; AGO and Coordinating Center for Clinical Trials, Marburg, Germany; University of Tuebingen, Department of Gynecology and Obstetrics, Tuebingen, Germany; AGO and Department of Gynecology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; AGO and Charité Campus Virchow-Klinikum, Berlin, Germany; Florence Nightingale Hospital, Düsseldorf, Germany; Department of Gynecology, Klinikum rechts der Isar der Technischen Universität, Munich, Germany; Department of Gynecology and Obstetrics, University Hospital Carl Gustav Carus, TU Dresden, Dresden, Germany; Imperial College London, London, United Kingdom; GINECO and Institut Bergonié, Bordeaux, France; GINECO and European Georges Pompidou Hospital, Paris, France; [Institut Claudius Regaud, IUCT-Oncopole, CRCT, Inserm, Toulouse, France](#); MITO and Istituto Nazionale Dei Tumori, Naples, Italy; University of Milano-Bicocca and Istituto Europeo di Oncologia, Milan, Italy; Mayo Clinic, Rochester, MN; Departments of Gynecology and Gynecologic Oncology, Kliniken Essen Mitte, Essen, Germany; AGO and Kliniken Essen Mitte, Essen, Germany

### [Abstract Disclosures](#)

Abstract:

**Background:** Primary cytoreductive surgery (PDS) followed by chemotherapy has been considered as standard management for advanced ovarian cancer patients (pts) over decades. An alternative approach of interval debulking surgery (IDS) following neoadjuvant chemotherapy (NACT) was subsequently reported by two randomized phase III trials (EORTC-GCG, CHORUS). Owing to important limitations of these studies, especially regarding surgical quality, optimal timing of surgical therapy in advanced ovarian cancer is still unclear. **Methods:** TRUST is an international open, randomized, controlled multicenter trial investigating overall survival (OS; primary endpoint) after PDS vs NACT and subsequent IDS in pts with FIGO stage IIIB-IVB ovarian, tubal, and peritoneal carcinoma. Secondary objectives are safety of complete tumor resection, progression-free survival and quality of life (QoL) as well as surgical morbidity. In order to guarantee adequate surgical quality, participating centers need to fulfill specific quality assurance criteria (e.g. ≥50% complete resection rate in upfront surgery for FIGO IIIB-IV pts, ≥36 debulking-surgeries/year) and agree to independent audits by TRUST Quality committee delegates. A 1:1 randomization to PDS or NACT followed by IDS stratified by center and age-ECOG combination (ECOG 0 and age ≤65 years vs ECOG > 0 or age > 65 years) is performed. Pts in the PDS arm will undergo surgery followed by 6 cycles of platinum-based chemotherapy, whereas pts in the IDS arm will be treated with 3 cycles of NACT after histologic confirmation of the disease, followed by IDS and subsequently 3 cycles of

platinum-based chemotherapy. Intention of surgery for both groups will be complete tumor resection as per guideline recommendations. Health related QoL will be assessed using the EORTC QLQ-C30, QLQ-OV28, and EQ-5D-3L questionnaires. For sample size planning, we considered a prolongation of median OS from 45 months in the IDS arm to 60 months in the PDS arm (HR 0.75) as clinically relevant. 380 events are needed to obtain a power of 80% in two-sided log-rank test with significance level of 0.05. The primary analysis will be done in the ITT-population of 686 randomized pts. By Feb 3 2017, 46 pts were randomized. Clinical trial information: [NCT02828618](https://clinicaltrials.gov/ct2/show/study/NCT02828618)