

IUCT Oncopole

1. Efficacy and tolerance of treatments received beyond progression in men with metastatic hormone-naïve prostate cancer treated with androgen deprivation therapy (ADT) with or without docetaxel in the GETUG-AFU 15 phase III trial.

Author(s): Pernelle Lavaud, Gwenaëlle Gravis, Clémence Legoupil, Florence Joly, Stéphane Oudard, Franck Priou, **Loïc Mourey**, Michel Soulié, Igor Latorzeff, Remy Delva, Ivan Krakowski, Brigitte Laguerre, Christine Theodore, Jean Marc Ferrero, Philippe Beuzeboc, Muriel Habibian, Stéphanie Foulon, Jean Marie Boher, Gabrielle Tergemina-Clain, Karim Fizazi; Gustave Roussy Cancer Campus, Villejuif, France; Medical Oncology, Institut Paoli Calmette, Hôpital de Jour, Marseille, France; Centre François Baclesse, Caen, France; Department of Medical Oncology, Hôpital Européen Georges Pompidou, Paris, France; Centre Hospitalier Départemental Les Oudairies, La Roche sur Yon, France; Institut Claudius Regaud, IUCT-O, Toulouse, France; Centre Hospitalier Universitaire Rangueil, Toulouse, France; Clinique Pasteur, Toulouse, France; Centre Paul Papin, Angers, France; Centre Alexis Vautrin, Vandœuvre-lès-Nancy, France; Centre Eugène Marquis, Rennes, France; Hospital Foch, Suresnes, France; Centre Antoine Lacassagne, Nice, France; Medical Oncology Department, Institut Curie, Paris, France; UNICANCER, Paris, France; Institut Gustave Roussy, Villejuif, France; Institut Paoli Calmettes, Marseille, France; Gustave-Roussy Cancer Campus, Biostatistics and Epidemiology unit, Villejuif, France; Institut Gustave Roussy, University of Paris Sud, Villejuif, France

Background: Since 2015, docetaxel chemotherapy, combined with ADT, is considered the standard of care in fit men with metastatic hormone-naïve prostate cancer (m-HNPC), based on data from three phase III trials (GETUG-AFU 15, CHAARTED, and STAMPEDE). No data are currently available regarding the treatments used beyond progression after upfront ADT and docetaxel. **Methods:** We retrospectively collected data from patients (pts) participating in the GETUG-AFU 15 phase III trial concerning treatments received beyond progression for castration-resistant disease (CRPC) in both arms (ADT and ADT + docetaxel) including treatment efficacy (measured by a PSA decline > 50%, physician assessment of clinical benefit, and time to events), and toxicity (NCI-CTC grading). **Results:** Data concerning 164 pts are currently available. The treatments most frequently used and their efficacy are detailed in the Table. Toxicity was mild, with only rare grade 3-4 events (16% with first treatments and 13% with second treatments used for CRPC) and no treatment-related death. **Conclusions:** In this retrospective analysis, anticancer activity was suggested with androgen receptor axis-targeted agents in patients with metastatic prostate cancer treated upfront with ADT + docetaxel. Rather limited activity was observed following a docetaxel rechallenge in this setting.

2. A phase I study of SAR566658, an anti CA6-antibody drug conjugate (ADC), in patients (Pts) with CA6-positive advanced solid tumors (STs)(NCT01156870).

Author(s): **Carlos Alberto Gomez-Roca**, Valentina Boni, Victor Moreno, John Charles Morris, **Jean-Pierre Delord**, Emiliano Calvo, Kyriakos P. Papadopoulos, Olivier Rixe, Patrick Cohen, Alexia Tellier, Samira Ziti-Ljajic, Anthony W. Tolcher; Institut Universitaire du Cancer de Toulouse, Toulouse, France; START Madrid, CIOCC, Madrid, Spain; START Madrid, FJD, Madrid, Spain; University of Cincinnati Cancer Institute, Cincinnati, OH; Institut Claudius Regaud, Toulouse, France; START San Antonio, San Antonio, TX; University of New Mexico Cancer Center, Albuquerque, NM; Sanofi R&D, Vitry-Sur-Seine, France

Background: SAR566658 (SAR) is a maytansinoid-loaded ADC targeting CA6, a sialoglycotope of MUC-1 over-expressed in solid tumors and rarely in normal tissues. **Methods:** Phase I dose escalation and expansion study to evaluate SAR intravenous administration as single agent every 3 weeks (q3w) and 2 weeks (q2w). Primary objective included dose limiting toxicities (DLTs), maximum tolerated dose (MTD) and recommended dose (RD). Secondary objectives were PK, PD and preliminary efficacy assessment (RECIST1.1). **Results:** One hundred and fourteen patients (Pts) with heavily pretreated solid tumors expressing CA6 in $\geq 30\%$ tumor cells with an intensity 2/3+ by immunohistochemistry were enrolled. SAR was administered across 11 dose levels (DLs) (10 to 240 mg/m² q3w and 120 mg/m² q2w). DLTs [1 grade (Gr) 3 diarrhea and 2 Gr3 keratitis] were observed at 240 mg/m². Initial RD was 190 mg/m² however a high incidence of keratopathy was seen mainly at cycle 2. PK/safety simulation, preserving drug exposure and limiting keratopathy incidence, proposed two alternative schedules: 90 mg/m² D1,D8 q3w and 120 mg/m² q2w. Most common adverse event (AE) was reversible Gr2/3 keratopathy in 41/114 (36%) (Gr3 in 9 Pts). Among these 41 Pts, 15/23 (65%) received 190 mg/m², 12/33 (36%) 150 mg/m², 6/8 (75%) 240 mg/m², 6/17 (35%) 90 mg/m² D1,D8 and 2/16 (13%) 120 mg/m² q2w. Prophylaxis with vasoconstrictor and steroids eye drops implemented in 8 patients in alternative schedules prevented keratopathy. Other AEs were fatigue (32.6%), peripheral neuropathy (31.6%), GI disorders [(nausea (29%), abdominal pain (26%), diarrhea (25%)] and neutropenia (2.6%). Low grade liver and renal abnormalities were noted. Tumor regression was noted in about 60% Pts at 190 and 90 mg/m² D1,D8 and 35% Pts at 150 and 120 mg/m² q2w. One complete response (ovary), 8 partial responses (3 breast, 2 ovary, 1 NSCLC, 1 cervix and 1 bladder) and 39% stable disease were noted. Highest overall response rate (ORR) was observed in 2/15 at 90 mg/m² D1,D8 and 3/23 at 190 mg/m². **Conclusions:** SAR 90 mg/m² D1,D8 q3w provided a favorable safety profile and encouraging antitumor activity and is selected as the RD for further clinical development.

3. Dose optimization of MK-8628 (OTX015), a small molecule inhibitor of bromodomain and extra-terminal (BET) proteins, in patients (pts) with recurrent glioblastoma (GB).

Author(s): Andreas Felix Hottinger, Marc Sanson, Elizabeth Moyal, Jean-Pierre Delord, Rita De Micheli, Keyvan Rezai, Abraham C.F. Leung, Susan Perez, Mohamed Bekradda, Nicolas Lachaux, Francois Marc Lokiec, Olivier L. Chinot; CHUV University Hospital, Lausanne, Switzerland; Groupe Hospitalier Universitaire Salpêtrière, Paris, France; Institut Claudius Regaud, IUCT-O, Toulouse, France; Institut Claudius Regaud, Toulouse, France; Centre Hospitalier Universitaire Vaudois and Lausanne University Hospital, Lausanne, Switzerland; Institut Curie-Hôpital René Huguenin, St Cloud, France; Genentech BioOnc, South San Francisco, CA; Merck Research Laboratories, Rahway, NJ; Oncology Therapeutic Development, Clichy, France; Institut Curie-Hopital Rene Huguenin, St Cloud, France; Aix-Marseille University, AP-HM, Service de Neuro-Oncologie, CHU Timone, Marseille, France

Background: Bromodomains (BRD) bind to acetylated lysine residues on histone tails and are directly involved in remodeling chromatin and regulating transcription, thus representing a potentially important anticancer target. MK-8628 is a synthetic small molecule targeting BRD2, 3 and 4 of the tandem-BRD-containing family of transcriptional regulators, the BET proteins. It has shown cytotoxic activity in *in vitro* GB models. We conducted a phase IIa trial with dose optimization to determine the MTD, safety and clinical activity of MK-8628 in pts with a first GB recurrence. **Methods:** In the first step, a traditional 3+3 dose escalation schema was used. At first recurrence of GB, pts were treated with MK-8628 administered orally at 3 dose levels (DL1: 80 mg QD, DL2: 120 mg QD, DL3: 160 mg QD) with 4-week cycles. PK analyses were performed on day 1 of cycle 1 and residual samples were drawn on day 28. MRI assessment was performed every 2 cycles (RANO). **Results:** Twelve pts were included between December 2014 and July 2015. M/F: 10/2, median age: 52 years (range: 31-70). Median time from diagnosis is 11 months (range 5-24), median KPS: 90%. Six pts were treated at DL1, 4 at DL2, and 2 at DL3. Pts received a median of 2 cycles of MK-8628 (range 1-4). Three pts had dose-limiting toxicity: 1 at DL1 (grade [G] 3 thrombocytopenia > 7 days) and 2 at DL3 (G3 thrombocytopenia > 7 days without bleeding; G3 hyperbilirubinemia lasting 2 days). Other drug-related toxicities included G3 thrombocytopenia (3 pts), G1-2 diarrhea (4 pts), G2 myalgia (1 pt), and G1 INR increase (1 pt). PK analysis in pts treated at the MTD (DL2) showed a mean C_{max} of 1813±270 nM with a mean AUC₍₀₋₂₄₎ of 7984±443 µg/L*h and T_{1/2} of 3.9±0.4 h. Best response was stable disease in 1 pt. All pts progressed, with a median PFS of 2 months (range, 1-4). **Conclusions:** Administration of MK-8628 is safe and well tolerated in pts with recurrent GB previously

exposed to alkylating agents and radiation therapy. The MTD was established at 120 mg MK-8628 QD with PK indicating that MK-8628 had reached biologically active levels. Given the lack of detectable clinical activity of MK-8628 in this population, the trial was closed.

4. A randomized, multicenter, open-label, phase II trial to evaluate the efficacy and safety of palbociclib in combination with fulvestrant or letrozole in patients with ER+/HER2- metastatic breast cancer (MBC).

Author(s): Antonio Llombart-Cussac, Meritxell Bellet, Pilar Zamora, Manuel Ruiz, Joseph Gligorov, Serena Di Cosimo, Peter Schmid, Shaheenah Dawood, Henri Roche, Frederic Marme, Elena Aguirre, Javier Cortes; Hospital Arnau Vilanova, Valencia, Spain; Hospital Universitari Vall D'Hebron, Barcelona, Spain; Department of Oncology, Hospital La Paz, Madrid, Spain; Hospital Universitario Virgen del Rocío, Sevilla, Spain; APHP Tenon, Med Oncology Dept, Paris, France; Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy; University of Sussex, London, United Kingdom; Medical Center, Breast Cancer Program, Dubai Hospital, Dubai, United Arab Emirates; Institut Universitaire du Cancer Toulouse - Oncopole, Toulouse, France; National Center for Tumor Disease/Department of Gynecology, University of Heidelberg, Heidelberg, Heidelberg, Germany; Medica Scientia Innovation Research (MedSIR), Barcelona, Spain

Background: Palbociclib (P) is a cyclin-dependent kinase inhibitor approved for the treatment of ER+/HER2- locally advanced (LA) or MBC and, in combination with endocrine therapy, was shown to be superior, in terms of PFS, to endocrine therapy alone in both a phase II trial comparing P+letrozole (L) to L alone (PALOMA-1) as well as in a phase III trial comparing P+ fulvestrant (F) to F alone (PALOMA-3). In the phase II FIRST study PFS was greater in the high-dose F (HDF) arm compared to anastrozole (A) as 1L therapy for ER+ MBC. The phase III FALCON study has recently completed accrual and compares HDF to A as 1L treatment. With two new (L+P and HDF) standards of care shaping up as 1L endocrine therapy for ER+/Her2- LA/MBC, exploring the combination of P+HDF in the 1L setting seems mandatory. **Methods:** The PARSIFAL phase II study is an open-label, randomized, controlled, multicenter study with the primary aim of assessing 1-year PFS of P+HDF vs. P+L in women with ER+ LA/MBC. 304 eligible pts will be enrolled in 53 centers and 9 countries (Europe and Middle East). Pts must be postmenopausal women > 18 years old, an ECOG score ≤ 2, and histologically confirmed recurrent ER+/HER2- LA/MBC. Pts may not have received prior chemotherapy for LA/MBC and are randomized to receive 125 mg capsules of P taken once daily from D1 to D21 of every 28D cycle together with either HDF 500 mg/5mL i.m. injection administered on D1 (Cycle 1 loading dose also requires D14 administration also on) or 2.5 mg tablets of L once daily from D1 to D28. Treatment is given until objective disease progression, symptomatic deterioration, unacceptable toxicity, death, or withdrawal of consent, whichever occurs first. For both combinations, secondary objectives are to: evaluate safety and tolerability; compare times to progression (TTP); and compare overall survival (OS) and clinical response results. The trial is in progress (start: Aug 2015, end: Jul 2017) and 62 pts have been accrued in 4 countries. A series of complementary prospective molecular studies are planned in order to evaluate predictive/prognostic biomarkers to P and endocrine therapy. Clinical trial information: 2014-004698-17.

5. An evaluation of the chronic lymphocytic leukemia (CLL) international prognostic index as a prognostic tool in patients with relapsed/refractory CLL in idelalisib phase 3 randomized studies.

Author(s): Jacob Drobnyk Soumerai, Jacqueline Claudia Barrientos, Michael Hallek, Thomas J. Kipps, Jeffrey Alan Jones, Stephan Stilgenbauer, Guan Xing, Nai-Shun Yao, Loic Ysebaert, Andrew David Zelenetz; Memorial

Sloan Kettering Cancer Center, New York, NY; Hofstra North Shore-LIJ School of Medicine, Hempstead, NY; Department of Internal Medicine and Center of Integrated Oncology, Cologne Bonn, University Hospital, Cologne, Germany; University of California San Diego/Moores Cancer Center, La Jolla, CA; The Ohio State University Comprehensive Cancer Center, Columbus, OH; University of Ulm, Ulm, Germany; Gilead Sciences, Inc., Foster City, CA; Department of Haematology, Institut Universitaire du Cancer de Toulouse- Oncopôle, Toulouse, France

Background: The International Prognostic Index for patients (pts) with CLL (CLL-IPI) is a validated scoring system with prognostic value for overall survival (OS) in untreated CLL, but it has not been studied in relapsed/refractory (R/R) CLL (Kutsch et al. *J Clin Oncol*.33 (suppl), 2015). The CLL-IPI is a risk-weighted model comprising the risk factors age (relative weight, 1), stage (1), del(17p)/TP53 mutation (-17p/TP53M) (4), IGHV mutation status (2), and β 2-microglobulin (2). We hypothesized that idelalisib (IDELA), an agent active in CLL with -17p/TP53M, can overcome the negative impact of high CLL-IPI risk on OS. **Methods:** The CLL-IPI score was analyzed in 460 pts with R/R CLL treated with IDELA + rituximab (R) vs placebo + R (NCT01539512) or IDELA + ofatumumab (O) vs O (NCT01659021). Subgroup analyses of OS were performed in 274 pts treated with IDELA + R or + O (IDELA cohort) and in 186 pts treated with R or O alone (control). Median OS was estimated for low, intermediate, high, and very high CLL-IPI risk groups using the Kaplan-Meier method. The log-rank test was used to compare survival distributions across groups and estimate hazard ratios (HRs) for OS. Results: At a median follow-up of 14.7 months, the CLL-IPI score was validated in the pooled cohort of all pts with R/R CLL, with significant differences in OS across CLL-IPI risk groups ($P=0.0001$; table). In the subgroup analysis, the CLL-IPI score was prognostic for OS in the control ($P=0.0007$) but not IDELA cohort ($P=0.0859$). Conclusions: Although low-risk pts are uncommon in the R/R setting, the CLL-IPI score is prognostic of OS in R/R CLL. IDELA partially overcomes the negative impact on OS of very high-risk disease driven by -17p/TP53M. Analyses of data derived from another phase 3 study are ongoing.

6. Expanded Access Program of GRASPA for treatment of patients with acute lymphoblastic leukemia unable to receive other form of L-Asparaginase: A status update (NCT02197650).

Author(s): Yves Bertrand, Herve Dombret, Bruno Quesnel, Severine Lissandre, Claudine Schmitt, Emmanuel Plouvier, Christian Recher, Maryline Poiree, Cecile DUMESNIL de MARICOURT, Iman El-Hariry; Institut d'Héματο-Oncologie Pédiatrique, Hospices Civils de Lyon, Lyon, France; Hôpital Saint Louis, Paris, France; Hopital Claude Huriez CHU Lille, Lille, France; CHU de Tours, TOURS, France; CHU Nantes, Nantes, France; CHR, Besancon, France; Hôpital Purpan-CHU de Toulouse, Toulouse, France; CHU Lenval, Nice, France; CHU Rouen, Rouen, France; Erytech, Cambridge, MA

7. Outcomes of patients with relapsed and refractory chronic lymphocytic leukemia (CLL) who discontinue idelalisib treatment.

Author(s): Jennifer R. Brown, Paolo Ghia, Jeffrey Alan Jones, Andrew Pettitt, Jeff Porter Sharman, Loic Ysebaert, Stephan Stilgenbauer, Yeonhee Kim, Terry Newcomb, Nai-Shun Yao, Richard R. Furman; Dana-Farber Cancer Institute, Boston, MA; Università Vita-Salute San Raffaele and IRCCS San Raffaele Scientific Institute, Milan, Italy; The Ohio State University, Columbus, OH; University of Liverpool, Department of Molecular and Clinical Cancer Medicine, Liverpool, United Kingdom; US Oncology Network/Willamette Valley Cancer Institute, Springfield, OR; Department of Haematology, Institut Universitaire du Cancer de Toulouse- Oncopôle, Toulouse, France; University of Ulm, Ulm, Germany; Gilead Sciences, Inc., Foster City, CA; Weill Cornell Medical College, New York, NY

Background: Idelalisib (IDELA) is effective in the treatment of patients (pts) with relapsed/refractory (R/R) CLL. Nonetheless, pts may discontinue (D/C) IDELA due to progressive disease (PD) or adverse events (AEs). In this post hoc analysis, we examined the outcomes of pts with R/R CLL who D/C IDELA and the relationship of these outcomes to IDELA exposure. **Methods:** Data were pooled for pts treated with IDELA + rituximab (NCT01539512, n = 110), IDELA monotherapy (NCT01539291, extension study), and IDELA + ofatumumab (NCT01659021, n = 173). Time-dependent endpoints, including time to next therapy (TTNT), time to PD (TTPD), and time to death (TTD), were calculated from the dates of permanent IDELA D/C. Kaplan-Meier analysis was used to estimate overall survival (OS) from the date of randomization. Subgroup analyses of OS were performed using the integrated safety data set. **Results:** Of 283 pts in the safety population, 124 (44%) remained on IDELA, 28 (10%) D/C due to PD, and 131 (46%) D/C for non-PD reasons (AEs, n = 87; "other" reasons, n = 44 [death, n = 7; study withdrawal, n = 21; physician's decision, n = 14; other, n = 2]). Clinical outcomes for these D/C groups (excluding "other") are presented in the table. Pts who D/C IDELA due to PD also had longer median IDELA exposure (11 vs 8 mo) than those who D/C due to AEs. **Conclusions:** Pts who were required to discontinue IDELA due to AEs survived no longer than those required to discontinue due to PD. OS was similar among pts who D/C IDELA, regardless of reason for D/C. Analyses of patient characteristics, type of PD and dose intensities associated with IDELA D/C, as well as outcomes based on timing of D/C due to AEs (early vs late), are ongoing.

8. Efficacy and safety of ixazomib plus lenalidomide-dexamethasone (IRd) vs placebo-rd in patients (pts) with relapsed/refractory multiple myeloma (RRMM) by cytogenetic risk status in the global phase III Tourmaline-MM1 study.

Author(s): Paul G. Richardson, Hervé Avet-Loiseau, Antonio Palumbo, Luisa Viterbo, Arnon Nagler, Peter Ganly, Dina Ben Yehuda, Jesus San Miguel, S.Vincent Rajkumar, Ludek Pour, Christian Langer, Nizar J. Bahlis, Andrzej Pluta, Tamas Masszi, Deborah Berg, Jianchang Lin, Helgi Van De Velde, Dixie-Lee Esseltine, Alessandra di Bacco, Philippe Moreau; Dana-Farber Cancer Institute, Boston, MA; University Cancer Center of Toulouse Institut National de la Santé, Toulouse, France; Myeloma Unit, Division of Hematology, University of Torino, Azienda Ospedaliera Citta' della Salute e della Scienza di Torino, Torino, Italy; Instituto Português de Oncologia do Porto Francisco Gentil, Porto, Portugal; Hematology Division, Chaim Sheba Medical Center, Tel-Hashomer, Israel; Christchurch Hospital, Christchurch, New Zealand; Hadassah Medical Center, Jerusalem, Israel; Clinica Universitaria de Navarra, Pamplona, Spain; Division of Hematology, Mayo Clinic, Rochester, MN; Hematology and Oncology, University Hospital Brno, Brno, Czech Republic; University Hospital Ulm, Ulm, Germany; Southern Alberta Cancer Research Institute, University of Calgary, Calgary, AB, Canada; Department of Hematological Oncology, Oncology Spec. Hospital, Brzozow, Poland; Department of Haematology and Stem Cell Transplantation, St. István and St. László Hospital of Budapest and Semmelweis University 3rd Department of Internal Medicine, Budapest, Hungary; Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA; University Hospital Hotel-Dieu, Nantes, France

Background: TOURMALINE-MM1 (NCT01564537) showed a significant 35% improvement in progression-free survival (PFS) with IRd vs placebo-Rd (hazard ratio [HR] 0.742, p = 0.012) in pts with RRMM (Moreau et al, ASH 2015). Here we present an analysis of the efficacy and safety of IRd vs placebo-Rd by cytogenetic status. **Methods:** Pts with RRMM were randomized 1:1 to receive IRd or placebo-Rd. High-risk cytogenetic abnormalities were assessed at a central laboratory; cut-off values were based on false-positive rates of the FISH probes, and were 5%, 3%, and 3% for del(17p), t(4;14), and t(14;16), respectively. Post-hoc analyses were performed using different cut-offs for del(17p) and t(4;14). **Results:** Of 722 pts enrolled, 552 (76%) had cytogenetic results (97% central laboratory-confirmed), of whom 137 had high-risk abnormalities (75 IRd, 62 placebo-Rd). PFS was improved with IRd vs placebo-Rd in high- and standard-risk pts (Table); in high-risk pts,

median PFS with IRd was similar to that in all pts and in standard-risk pts. PFS benefit with IRd vs placebo-Rd was consistent using different positivity cut-offs of 20% del(17p) (n = 59; median 21.4 vs 6.7 mos, HR 0.611), 60% del(17p) (n = 33; median 15.7 vs 5.1 mos, HR 0.49), and 10% t(4;14) alone (n = 59; median 18.5 vs 12.0 mos, HR 0.444). Median TTP with IRd vs placebo-Rd was 21.4 vs 12.0 mos and 20.6 vs 15.9 mos in high- and standard-risk pts. Overall response rate (CR+VGPR rate) with IRd vs placebo-Rd was 79% vs 60% (45% vs 21%) and 80% vs 73% (51% vs 44%) in high- and standard-risk pts. Rates of grade ≥ 3 AEs with IRd vs placebo-Rd were 66% vs 73% in high- and 75% vs 65% in standard-risk pts; rates of serious AEs were 42% vs 52% and 45% vs 47%, respectively. **Conclusions:** IRd showed substantial benefit vs placebo-Rd in RRMM pts with high-risk cytogenetic abnormalities, irrespective of the cut-offs used, with limited additional toxicity.

9. Vismodegib (VISMO), a hedgehog pathway inhibitor (HPI), in advanced basal cell carcinoma (aBCC): STEVIE study primary analysis in 1215 patients (pts).

Author(s): Johan Hansson, Axel Hauschild, Rainer Kunstfeld, Jean Jacques Grob, Brigitte Dréno, Laurent Mortier, Paolo Antonio Ascierto, Lisa F. Licitra, Caroline Dutriaux, Luc Thomas, **Nicolas Meyer**, Bernard Guillot, Reinhard Dummer, Petr Arenberger, Kate Fife, Ana Raimundo, Emi Dika, Natalie Dimier, Ioannis Xynos, Nicole Basset-Seguín; Karolinska Institute and Karolinska University Hospital, Stockholm, Sweden; University of Kiel, Kiel, Germany; Medical University of Vienna, Vienna, Austria; CHU Timone APHM, Aix-Marseille University, Marseille, France; Nantes University, Nantes, France; Université Lille, Centre Hospitalier Régional Universitaire de Lille, Lille, France; Istituto Nazionale Tumori Fondazione Pascale, Naples, Italy; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Hôpital Saint-André, CHU Bordeaux, Bordeaux, France; Lyon 1 University Centre Hospitalier Lyon Sud, Pierre Benite, France; Institut Universitaire du Cancer de Toulouse, Paul Sabatier University, Toulouse, France; CHU Montpellier, Montpellier, France; University Hospital Zurich, Zurich, Switzerland; University Hospital Kralovske Vinohrady Prague and Charles University Third Medical Faculty, Prague, Czech Republic; NIHR Cambridge Biomedical Research Centre, Cambridge, United Kingdom; Instituto Português de Oncologia Porto, Porto, Portugal; University of Bologna, Bologna, Italy; Roche Products Ltd., Welwyn Garden City, United Kingdom; Dermatology Department, Hôpital Saint-Louis, Assistance-Publique-Hôpitaux de Paris, Paris, France

Background: VISMO, a first-in-class HPI, is approved (US and EU) for use in adults with aBCC. STEVIE is an open-label study focusing on safety of VISMO in pts with aBCC in a real-world setting. We present data from the primary analysis. **Methods:** Adult pts (laBCC, mBCC) received oral VISMO 150 mg QD until progressive disease, unacceptable toxicity, or withdrawal. Primary objective is safety; pts are followed for 12 months after last dose of VISMO. Secondary objectives include efficacy and quality of life. **Results:** This analysis includes 1215 pts (laBCC, n = 1119; mBCC, n = 96) at 165 sites in 36 countries. Median (range) age was 72.0 (18.0-101.0) yrs. At the time of analysis, 375 (31%) patients remained on study. Median (range) treatment duration was 8.6 (0-44) months. Treatment-emergent AEs (TEAEs) included muscle spasm (66.4%), alopecia (61.5%), dysgeusia (54.6%), decreased weight (40.6%), decreased appetite (24.9%), asthenia (24.0%), nausea (17.9%), and ageusia (17.5%). Serious TEAEs occurred in 289 pts (23.8%). There was no trend of increased TEAEs or grade ≥ 3 TEAEs with increased time on treatment adjusted by pt-yr. Forty-six pts died from grade 5 TEAEs. Seven deaths were considered by investigator (INV) to be related to VISMO (2 myocardial infarction, 1 each of cardiorespiratory arrest, pancreatitis, pulmonary embolism, ischemic stroke, renal failure; all involved confounding factors). Best overall response (RECIST 1.1; INV-assessed) in pts with histologically confirmed measurable baseline disease (laBCC, n = 1077; mBCC, n = 84) included complete response (CR) (33.4% laBCC; 4.8% mBCC) and partial response (35.1% laBCC; 32.1% mBCC). Median duration of response was 23.0 (95% confidence interval [CI]: 20.4, 26.7) and 13.9 (95% CI: 9.23, not estimable) months in pts with laBCC and mBCC, respectively. Median progression-free survival was 23.2 (95% CI: 21.4, 26.0) and 13.1 (95% CI: 12.0, 17.7) months in pts with laBCC and mBCC, respectively. **Conclusions:** The primary analysis of STEVIE, the largest ever clinical trial in pts with

aBCC, confirms the previously observed safety profile and high response rates with VISMO, including many CRs as well as durable responses.

10. Long term toxicity and fatigue after treatment for non-Hodgkin lymphoma (NHL): An analysis of twelve collaborative lymphoma study association (LYSA) trials, the Simonal Study.

Author(s): Nicolas Mounier, Sabine Anthony, Raphael Busson, Catherine Thieblemont, Virginie Nerich, Vincent Ribrag, Marie Castera, Herve Tilly, Corinne Haioun, Rene-Olivier Casasnovas, Franck Morschhauser, Pierre Feugier, Richard Delarue, Loic Ysebaert, Catherine Sebban, Florence Broussais, Gandhi Damaj, Jean-Philippe Jais, Michel Henry-Amar, Gilles A. Salles; CHU l'Archet, Nice, France; CHU Nice, Nice, France; Universite de Caen-Basse Normandie, Caen, France; CHU St Louis, Paris, France; Institut Régional Federatif de Cancerologie, Besançon, France; Institut Gustave Roussy, Villejuif, France; CLCC Baclesse, Caen, France; Centre Henri Becquerel, Rouen, France; CHU Henri Mondor, Créteil, France; Department of Hematology, Hôpital Le Bocage, Dijon, France; CHU Lille- Hopital Claude Huriez, Lille, France; CHU Nancy, Nancy, France; AP-HP Hopital Universitaire Necker Enfants Malades, Paris, France; Department of Haematology, Institut Universitaire du Cancer de Toulouse- Oncopôle, Toulouse, France; CLCC Berart, Lyon, France; LYSA-RC, Lyon, France; Department of Hematology, University Hospital, School of Medicine, Caen, France; Universite Paris Descartes, Paris, France; University De Lyon, Hospices Civils De Lyon, Lyon, France

Background: NHL survivors are at high risk for second cancers (SC) and late toxicities such as cardiovascular (CV) or neuro-psychiatric (NP) disorders. Little is known about new agents such as rituximab (RITUX). The impact of treatment regimens on late morbidity was analyzed in a large cohort of survivors with long follow-up (FU). **Methods:** In 2015, a fatigue (MFI-20) and a self-assessment Life Situation Questionnaire (LSQ) were mailed to survivors treated in 12 successive LYSA randomized trials (1993-2007) for Diffuse Large B cell (DLBCL) and follicular (FL) lymphomas. Of 8113 pts enrolled into trials, 5247 were alive at last FU. Addresses were obtained for 3317 survivors of whom 1671 (50%) returned the questionnaires. Responders more often came from recent trials and were more often treated with RITUX than non-responders. NHL prognostic factors and chemotherapy were similar in both groups. Linear regression models were used to assess factors linked to increased fatigue level. **Results:** There were 906 males and 765 females (median age 64 yrs; 24 to 95). 28% had FL and 72% DLBCL. 811 pts received CHOP-like chemotherapy, 518 high-dose CHOP and 342 up-front autograft consolidation (ASCT). RITUX was combined to chemotherapy in 829 pts (50%). Median FU was 11 yrs (5 to 23). 583 pts (35%) reported no morbidity. For the remaining, late events (1 to 7) were: CV in 20%, NP in 17%, infections in 12%, musculoskeletal (MSk) disorders in 11%, pulmonary (Pulm) diseases in 8%, digestive diseases in 5% and SC in 8%. RITUX was associated with less SC (6 vs 9%, $p = 0.02$) and less CV (17 vs 23%, $p = 0.006$). Up-front ASCT was associated with more infections (17 vs 11%, $p = 0.002$) and more Pulm (12 vs 7%, $p = 0.005$). Age above 75 (20%) was only associated with more CV and more SC. 1036 pts (64%) expressed persistent fatigue (MFI score ≥ 40). There were no significant impact of any treatments. Increased fatigue level was associated ($p < 0.001$) with age, obesity, CV, Pulm, MSk and NP. **Conclusions:** This first study reporting on long-term NHL survivors confirms an altered health status. Initial combination of chemotherapy and RITUX does not increase late morbidity and fatigue. Clinical trial information: pooled trials already registered.

11. Validation of the new glioma WHO classification in the french POLA network: Analysis of 1041 cases.

Author(s): Emeline Tabouret, Anh Tuan Nguyen, Caroline Dehais, Catherine Carpentier, Laura Lebouil, François Ducray, Ahmed Idbaih, Karima Moktari, Anne Jouvret, Emmanuelle uro-Coste, Jean-Yves Delattre, Dominique Figarella-Branger; Aix-Marseille University, AP-HM, Service de Neuro-Oncologie, CHU Timone, Marseille,

France; Hopital Sainte Anne, Toulon, France; Pitie-Salpetriere Hospital- Pierre et Marie Curie Paris VI University, Paris, France; Institut Du Cerveau et de La Moelle - Groupe Hospitalier Pitié Salpêtrière, Paris, France; Groupe Hospitalier Pitié-Salpêtrière, Paris, France; Hopital Pierre Wertheimer, Lyon, France; Universite Pierre et Marie Curie Paris VI, Paris, France; Groupe Hospitalier Pitié-Salpêtrière, Paris, France; CHU Toulouse, Toulouse, France; Pitie-Salpetriere Hospital-Pierre et Marie Curie Paris VI University, Paris, France; Aix-Marseille University, AP-HM, Service d'Anatomopathologie et de Neuropathologie, CHU Timone, Marseille, France

Background: The upcoming WHO classification of gliomas will be refined taking into account the robust molecular alterations of gliomagenesis: the 1p19q codeletion and *IDH1/2* mutations. **Methods:** All cases of high-grade oligodendroglial tumors sent for central pathological review and included into the French nation-wide POLA network were reclassified according the upgrading of the 4th WHO classification that integrates pathological features and molecular data. Immunohistochemical expression of IDH1R132H, and ATRX, 1p19q codeletion, chromosome 7p gain and chromosome 10q loss by genomic-array and *IDH1/2* and histone K27M mutational statuses by sequencing were evaluated. **Results:** 1041 patients were included with a median age at diagnosis of 50.4 years (range, 17.1-84.4). Based on the new histo-molecular classification, diagnoses were: anaplastic oligodendroglioma with 1p19q codeletion (32.5%), anaplastic astrocytoma *IDH* mutated (*IDHmt*) (11.0%), anaplastic astrocytoma *IDH*wild-type (*IDHwt*) (5.3%), glioblastoma *IDHmt* (17.1%) and glioblastoma *IDHwt* (33.2%). Ten patients presented a midline tumor with the histone H3-K27M mutation. Both new and oldest WHO classifications were predictive for Progression-Free Survival (PFS) and Overall Survival (OS) but the new histo-molecular classification was more discriminant with higher hazard ratio for PFS (1.603, 1.848, 5.025 and 6.135 versus 1.495, 2.705, 2.799 and 4.933) and for OS (3.588, 3.493, 11.020 and 14.708 versus 2.259, 4.340, 4.214 and 7.534). Grading (III versus IV) was not prognostic for *IDHmt* non 1p19q codeleted gliomas in univariate analyses (PFS, $p=0.5$; OS, $p=0.8$) and multivariate analysis (adjusted by age, type of surgery and first line treatment: PFS, $p=0.13$; OS, $p=0.38$). Among anaplastic astrocytoma *IDHwt*, cases presenting with 7p gain and 10q loss (55%) had a worse prognosis than the others for PFS ($p=0.027$), suggesting that all anaplastic astrocytoma/*IDHwt* should not be considered as glioblastoma *IDHwt*. **Conclusions:** WHO histo-molecular classification of gliomas presented with high predictive and discriminative value, allowing the validation of three main molecular subgroups for the future neuro-oncological trials.

12. Updated results of a phase III randomized, controlled study of idelalisib in combination with ofatumumab for previously treated chronic lymphocytic leukemia (CLL).

Author(s): Jeffrey Alan Jones, Tadeusz Robak, Malgorzata Wach, Jennifer R. Brown, Alexander R. Menter, Elizabeth Vandenberghe, Loic Ysebaert, Nina D. Wagner-Johnston, Jonathan Polikoff, Farrukh Tauseef Awan, Xavier Camille Albert Badoux, Steven Coutre, Stephen Edward Forbes Spurgeon, Javier Loscertales, Lyndah Dreiling, Guan Xing, Sissy Peterman, Ronald L. Dubowy, Ian Flinn, Carolyn Owen; The Ohio State University Comprehensive Cancer Center, Columbus, OH; Medical University of Lodz, Lodz, Poland; Medical University of Lublin, Lublin, Poland; Dana-Farber Cancer Institute, Boston, MA; Kaiser Permanente Medical Group, Denver, CO; Saint James's Hospital, Dublin, Ireland; CHU Toulouse, Toulouse, France; The Johns Hopkins Hospital, Baltimore, MD; Kaiser Hospital San Diego, San Marcos, CA; St George Hospital, Cammeray, Australia; Stanford University, Stanford, CA; Oregon Health and Science University, Portland, OR; Hospital Universitario La Princesa, Madrid, Spain; Gilead Sciences, Inc., Foster City, CA; Hematologic Malignancies Research Program, Sarah Cannon Research Institute, Nashville, TN; Alberta Health Services, Calgary, AB, Canada

Background: Idelalisib (IDELA) is an oral PI3K δ inhibitor approved for use with rituximab in pts with relapsed CLL. This open-label study (NCT01659021) compared IDELA + ofatumumab (OFA) v OFA in pts with relapsed CLL. Results of the primary (1^o) endpoint analysis were previously reported (Jones et al, ASCO 2015) and are

updated here with an additional 8.5 mos of follow-up. In the 1° analysis, the combination yielded superior PFS and the KM estimated median OS was 20.9 and 19.4 mos in the IDELA+OFA and OFA arms. **Methods:** Pts with CLL progressing ≤ 24 mo from last therapy, who had received ≥ 2 cycles of a purine analogue or bendamustine, were randomized 2:1 to either Arm A (IDELA 150 mg BID continuously plus OFA, 300 mg IV wk 1, then 1 g IV q wk x 7 and q 4 wk x 4) or Arm B (OFA, same as Arm A except 2 g was substituted for 1 g dosing) with stratification factors relapsed v refractory, del17p and/or TP53 mutation, and *IGHV* mutation. The 1° endpoint was PFS based on IRC using modified IWCLL 2008 criteria. **Results:** Pt characteristics were balanced in the 2 arms: med age 67; Rai II/III/IV 18/13/51%, med no. prior regimens 3, refractory 49%, del17p/*TP53*mut 40%, *IGHV* unmut 78%. Exposure, disposition, and efficacy are shown in the table. Results were consistent across risk groups. Gr ≥ 3 AEs in Arm A included diarrhea/colitis (23.1%), pneumonia (19.7%), and pneumonitis (4.6%). **Conclusions:** With > 8 mos longer follow-up, IDELA + OFA vs OFA continues to show superior PFS and ORR, and now demonstrates superior OS in pts with del17p/*TP53*mut and a trend of improvement of OS in the ITT population.

13. Lenalidomide (LEN) maintenance (MNTC) after high-dose melphalan and autologous stem cell transplant (ASCT) in multiple myeloma (MM): A meta-analysis (MA) of overall survival (OS).

Author(s): Michel Attal, Antonio Palumbo, Sarah A. Holstein, Valerie Lauwers-Cances, Maria Teresa Petrucci, Paul G. Richardson, Cyrille Hulin, Patrizia Tosi, Kenneth Carl Anderson, Denis Caillot, Valeria Magarotto, Philippe Moreau, Gerald Marit, Zhinuan Yu, Philip L. McCarthy; CHU Purpan, Toulouse, France; Department of Hematology, University of Torino, Torino, Italy; Roswell Park Cancer Institute, Buffalo, NY; University La Sapienza, Rome, Italy; Department of Hematology, Sapienza University of Rome, Rome, Italy; Dana-Farber Cancer Institute, Boston, MA; Hematology Department, University Hospital, Nancy, France; Seràgnoli Institute of Hematology and Medical Oncology, Bologna University, Bologna, Italy; Dijon University Hospital Center, Dijon, France; Myeloma Unit, Division of Hematology, University of Torino, AOU S. Giovanni Battista, Torino, Italy; University Hospital Hotel-Dieu, Nantes, France; Service d'Hématologie Clinique, Hôpital du Haut Leveque CHU de Bordeaux, Bordeaux, France; Celgene Corporation, Summit, NJ

14. SHIVA: Randomized phase II trial comparing molecularly targeted therapy based on tumor molecular profiling versus conventional therapy in patients with refractory cancer—PFS ratio from patients who crossed-over.

Author(s): Christophe Le Tourneau, Maud Kamal, Cecile Mauborgne, Fabrice Mulot, Jean-Pierre Delord, Anthony Goncalves, Celine Gavoille, Coraline Dubot, Nicolas Isambert, Mario Campone, Olivier Tredan, Francesco Ricci, Marie Alt, Delphine Loirat, Marie-Paule Sablin, Xavier Paoletti, Vincent Servois, Lisa Belin; Institut Curie, Paris, France; Institut Claudius Regaud, Toulouse, France; Department of Medical Oncology, Institut Paoli-Calmettes, Marseille, France; Institut de Cancérologie de Lorraine, Département d'Oncologie Médicale, Nancy, France; Hôpital René Huguenin/Institut Curie, Saint-Cloud, France; Centre Georges François Leclerc, Dijon, France; Cancer Institute of the West (ICO), Centre René Gauducheau, Medical Oncology Department, Saint-Herblain,

France; Département d'Oncologie Médicale, Centre Léon Bérard, Lyon, France; Medical Oncology, Institut Curie, Paris, France; Institut Gustave Roussy, Villejuif, France

Background: Several studies used the ratio of progression-free survival (PFS) on genotype-matched treatment to PFS on genotype-unmatched treatment to assess the efficacy of therapy guided by patients' tumor molecular profiling [von Hoff et al., JCO 2010; Tsimberidou et al., CCR 2012]. We evaluated the PFS ratio from patients included in the SHIVA trial who crossed-over [Le Tourneau et al., Lancet Oncol 2015] (NCT01771458). **Methods:** The primary endpoint of the SHIVA trial was to compare PFS on molecularly targeted agents (MTAs) based on tumor molecular profiling and treatment at physician's choice (TPC) in patients with any kind of cancer who had failed standard-of-care therapy. Experimental treatment included only marketed MTAs given outside their indications according to a pre-specified treatment algorithm. Patients were allowed to cross-over at disease progression. Response was evaluated according to RECIST 1.1 at randomization and at cross-over. We evaluated the proportion of patients with a PFS ratio (PFS2 on MTA/PFS1 on TPC) > 1.3 among the patients who crossed-over from the TPC arm to the MTA arm, using each patient as his/her own control. Patients with a censored PFS2 were considered as having progressive disease. **Results:** Among 741 patients enrolled in the SHIVA trial, 197 were randomized, and 95 crossed-over at disease progression, including 70 patients from TPC arm to MTA arm and 25 patients from MTA arm to TPC arm. Two patients crossed-over in the control arm without disease progression. Among the 68 patients who crossed-over from TPC arm to MTA arm with disease progression, median PFS1 was 2.0 months and median PFS2 was 2.1 months. The PFS ratio exceeded 1.3 in 35% of patients [95%CI: 24 - 46], including 20% of patients with PFS ratio > 2. The PFS ratio was 1-1.3, 0.7-1.0 and < 0.7 in 13%, 25%, and 26% of patients, respectively. **Conclusions:** We report a PFS ratio > 1.3 in 35% of patients who crossed-over from the TPC arm to the MTA arm in the randomized SHIVA trial, suggesting a clinical benefit of the evaluated histology-agnostic approach in this subgroup of patients

15. Avelumab (MSB0010718C; anti-PD-L1) in patients with advanced unresectable mesothelioma from the JAVELIN solid tumor phase Ib trial: Safety, clinical activity, and PD-L1 expression.

Author(s): Raffit Hassan, Anish Thomas, Manish R. Patel, John J. Nemunaitis, Jaafar Bennouna, John D. Powderly, Matthew H. Taylor, Afshin Dowlati, Franklin Chen, Joseph Leach, Ulka N. Vaishampayan, Claire F. Verschraegen, **Jean-Pierre Delord**, Hans Juergen Grote, Anja von Heydebreck, Jean-Marie Cuillerot, James L. Gulley; Thoracic and Gastrointestinal Oncology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD; Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD; Sarah Cannon Research Institute/Florida Cancer Specialists, Sarasota, FL; Mary Crowley Cancer Research Centers, Dallas, TX; Institut de Cancérologie de l'Ouest – site René Gauducheau, Saint Herblain, France; Carolina BioOncology Institute, Huntersville, NC; Knight Cancer Institute, Oregon Health and Science University, Portland, OR; University Hospitals Seidman Cancer Center, Case Western Reserve University, Cleveland, OH; Novant Health Oncology Specialists, Winston-Salem, NC; Virginia Piper Cancer Institute, Minneapolis, MN; Karmanos Cancer Institute, Detroit, MI; University of Vermont, Burlington, VT; Institut Claudius Regaud, Toulouse, France; Merck KGaA, Darmstadt, Germany; EMD Serono, Billerica, MA; Genitourinary Malignancies Branch, National Cancer Institute at the National Institutes of Health, Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD

Background: Avelumab* is a fully human anti-PD-L1 IgG1 antibody under clinical investigation in multiple cancers. We report safety and clinical activity of avelumab in patients (pts) with unresectable mesothelioma

(NCT01772004). **Methods:** Pts with unresectable pleural or peritoneal mesothelioma, progressed after a platinum-pemetrexed-containing regimen and unselected for PD-L1 expression, were treated with avelumab 10 mg/kg IV Q2W until progression, unacceptable toxicity, or withdrawal. Tumors were assessed every 6 wks (RECIST 1.1). Objective response rate (ORR) and progression-free survival (PFS) were evaluated. Adverse events (AEs) were graded by NCI CTCAE v4.0. PD-L1 expression was assessed by IHC. **Results:** As of Oct 23, 2015, 53 pts were treated with avelumab and followed for a median of 46 wks (range 11-59). Median age was 66 y (range 32-84), ECOG PS was 0 (26.4%) or 1 (73.6%), median number of prior treatments was 1.5 (range 0-7). Histology was epithelial (81.1%), mixed (11.3%), sarcomatoid (3.8%), or unknown (3.8%). Treatment-related (TR) AEs occurred in 41 pts (77.4%); most common (>10%) were infusion-related reaction (20 [37.7%]), fatigue (8 [15.1%]), chills (8 [15.1%]), and pyrexia (6 [11.3%]), all of grade 1/2. Grade ≥ 3 TRAEs occurred in 4 pts (7.5%); colitis, decreased lymphocytes, and increased GGT or CPK [each 1 event]; there were no treatment-related deaths. Unconfirmed ORR was 9.4% (5 PRs; 95% CI: 3.1, 20.7); 4 were ongoing. Stable disease was observed in 25 pts (47.2%); disease control rate was 56.6%. Median PFS was 17.1 wks (95% CI: 6.1, 30.1), and PFS rate at 24 wks was 38.4% (95% CI: 23.3, 53.4). Using a $\geq 5\%$ cutoff for tumor cell staining, 14/39 evaluable (35.9%) were PD-L1+, ORR was 14.3% in PD-L1+ (2/14) vs 8.0% in PD-L1- pts (2/25), and median PFS was 17.1 wks (95% CI: 5.4, ne) in PD-L1+ vs 7.4 wks (95% CI: 6.0, 30.1) in PD-L1- pts. **Conclusions:** Avelumab showed an acceptable safety profile and clinical activity in PD-L1+ and PD-L1- pts with advanced unresectable mesothelioma, a dataset representing the largest study to date of an all-comer population in this tumor type treated with anti-PD-(L)1. *

16. Phase III non-inferiority study of cabazitaxel (C) 20 mg/m² (C20) versus 25 mg/m² (C25) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) previously treated with docetaxel (D).

Author(s): Johann S. De Bono, Anne-Claire Hardy-Bessard, Choung-Soo Kim, Lajos Geczi, Daniel Ford, Loic Mourey, Joan Carles, Phillip Parente, Albert Font, Gabriel Kacso, Mustapha Chadjaa, Wenping Zhang, François Ravez, Mario A. Eisenberger; The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research, London, United Kingdom; Centre Armorica d'Oncologie, Cario, Plérin, France; Asan Medicine Center, Seoul, South Korea; National Institute of Oncology, Budapest, Hungary; City Hospital, Cancer Centre Queen Elizabeth Hospital, Birmingham, United Kingdom; Institut Claudius Regaud, IUCT-O, Toulouse, France; Vall d'Hebron University Hospital, Barcelona, Spain; Eastern Health Clinical School, Monash University, Melbourne, Australia; Institut Català d'Oncologia, Hospital Universitari Germans Trias i Pujol, Badalona, Spain; Amethyst Radiotherapy Center, Cluj, Romania; Sanofi, Paris, France; Sanofi, Bridgewater, NJ; The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD

Background: The Phase III TROPIC study (NCT00417079) reported a significant improvement in overall survival (OS) for C plus prednisone (P) (25 mg/m² once every 3 weeks plus 10 mg orally once daily) versus mitoxantrone plus P (Hazard Ratio [HR] 0.70; P < 0.0001) in pts with mCRPC previously treated with D. This PROSELICA study (NCT01308580) was designed to determine the relative efficacy and safety profile of C20 plus P compared with C25 plus P. **Methods:** In this randomized, open-label, multinational phase III study, pts with mCRPC and ECOG performance status 0–2, who progressed after treatment with D, were stratified (ECOG, RECIST, region) and randomized 1:1 to C20 or C25. To show that C20 could preserve $\geq 50\%$ of the efficacy benefit showed by C25 in TROPIC, the HR of C20 vs C25 for the primary endpoint OS could not exceed 1.214 under 1-sided 98.89% confidence level adjusted after interim analyses. Secondary endpoints included progression free survival (PFS), safety, PSA, pain and tumor responses and quality of life. **Results:** From April 2011 to December 2013, 1200 pts were randomized (C20 n = 598; C25 n = 602). Patient characteristics were similar for C20 and C25. Median number of C cycles was 6 for C20 and 7 for C25. The median survival of C20 and C25 did not differ significantly and the HR boundaries (99% confidence level) were within the non-inferiority margins assumptions, therefore meeting the study's non-inferiority endpoint. PSA and RECIST response rates were higher in C25 (see

Table). Grade 3–4 adverse events: 39.7% C20; 54.5% C25. Grade 4 laboratory neutropenia: 21.3% C20; 48.6% C25. Neutropenic sepsis/infection: 2.2% C20; 6.1% C25. **Conclusions:** In pts with mCRPC progressing after treatment with D, C20 demonstrates non-inferiority for OS compared with C25 and an improved overall safety profile

17. Overall survival of patients with HER2-negative metastatic breast cancer treated with a first-line paclitaxel with or without bevacizumab in real-life setting: Results of a multicenter national observational study.

Author(s): Suzette Delalogue, David Pérol, Etienne Brain, Bernard Asselain, Thomas Denis Bachelot, Marc Debled, Veronique Dieras, Mario Campone, Christelle Levy, William Jacot, Veronique Lorgis, Corinne Veyret, Florence Dalenc, Jean-Marc Ferrero, Lionel Uwer, Anthony Goncalves, Irwin Piot, Gaetane Simon, Mathieu Robain, Christian Cailliot; Institut Gustave Roussy, Villejuif, France; Centre Léon Bérard, Lyon, France; Centre Rene Huguenin, St Cloud, France; Institut Curie, Paris, France; Institut Bergonie, Bordeaux, France; Cancer Institute of the West (ICO), Centre René Gauducheau, Medical Oncology Department, Saint-Herblain, France; Centre François Baclesse, Caen, France; Institut du Cancer de Montpellier, Montpellier, France; Centre Georges-François Leclerc, Dijon, France; Department of Medical Oncology, Henri Becquerel Center, Rouen, France; Institut Claudius Regaud, Toulouse, France; Department d'Oncologie Medicale, Centre Antoine Lacassagne, Nice, France; Centre Alexis Vautrin, Nancy, France; Department of Medical Oncology, Institut Paoli-Calmettes, Marseille, France; UNICANCER, Paris, France

Background: In 2014, UNICANCER (composed of 18 French Comprehensive Cancer Centers) launched the Epidemiological Strategy and Medical Economics (ESME) program to centralize real-world data in oncology. Metastatic breast cancer (mBC) was first selected to address the value of bevacizumab (B) added to paclitaxel (P) as first-line chemotherapy (CT) for HER2-negative tumours, while randomized trials have led to mixed results on outcome. **Methods:** The ESME-mBC database was built from information systems, treatment databases and patients' electronic files including quality control processes. All patients who started a first-line anti-cancer treatment for mBC between 01-Jan-2008 and 31-Dec-2013 were selected. The primary objective of the present study was to assess overall survival (OS) in patients with HER2-mBC treated with a first-line P-based CT ± B. Cox regression with adjustment for the main prognostic covariates was used to estimate the hazard ratio (HR) for OS and progression-free survival (PFS). To adjust for confounders, advanced methodological methods including propensity score, matching factor for nested case-control analyses and sensitivity analyses were performed. **Results:** Among 14,014 patients recorded in the ESME-mBC database, 10,605 had HER2-negative tumors. Of these, 2,127 and 1,299 received P+B and P respectively as first-line CT. OS was significantly higher in the P+B group compared with P alone (HR = 0.672 [95%CI, 0.601;0.752]; median survival time, 27.7 versus 19.8 months). Results were consistent across all supportive and sensitivity analyses, including in triple-negative and estrogen receptor-positive tumors subgroups. PFS was also higher for those receiving P+B versus P (HR = 0.739 [0.672; 0.813]; 8.1 versus 6.4 months). **Conclusions:** In this large-scale real-life setting database, patients with HER2-negative mBC who received P+B had a significantly better OS and PFS than those receiving P alone. Despite robust methodology, real-world data should be interpreted with caution. However, these data shed light on the potential interest of real-life data in oncology.

18. Does short-term androgen depletion add to high dose radiotherapy (80 Gy) in localized intermediate

risk prostate cancer? Final analysis of GETUG 14 randomized trial (EU-20503/NCT00104741).

Author(s): Bernard M. Dubray, Julia Salleron, Stephane Gilles Guerif, Elisabeth Le Prise, Agnes Reynaud-Bougnoux, Jean-Michel Hannoun-Levi, Tan Dat Nguyen, Christophe Hennequin, Jacques Cretin, Maryse Fayolle-Campana, Jean-Leon Lagrange, Jean-Marc Bachaud, David Azria, Alain Grangirard, Pascal Pommier, Jean-Marc Simon, Muriel Habibian, Pierre Bey, Veronique Beckendorf, Groupe d'Etude des Tumeurs Uro-Génitales (GETUG); CRLCC Henri Becquerel, Rouen, France; Institut de Cancérologie de Lorraine, Nancy, France; University Hospital of Poitiers, Poitiers, France; Centre Eugene Marquis, Rennes, France; CHU Bretonneau, Tours, France; Centre Antoine-Lacassagne, Nice, France; Institut Jean-Godinot, Reims, France; Dept of Radiation Oncology, Hôpital Saint-Louis, Paris, France; Clinique Valdegour, Nimes, France; HIA Val de Grace, Paris, France; CHU Henri Mondor, Creteil, France; CRLCC Claudius Regaud, Toulouse, France; Institut Régional du Cancer, Montpellier, France; Hopital du Hasenrain, Mulhouse, France; CRLCC Léon Bérard, Lyon, France; CHU Pitie-Salpetriere, Paris, France; UNICANCER, Paris, France; Institut de Cancérologie de Lorraine, Vandoeuvre-Lès-Nancy, France

Background: Multi-center randomized trial to evaluate the addition of 4-month androgen deprivation to high dose radiotherapy in intermediate risk localized prostate adenocarcinoma patients (pts). **Methods:** eligible pts were randomly assigned to high dose conformal radiotherapy (prostate 80 Gy / 40 fractions; seminal vesicles 46 Gy / 23 fractions) either alone (group RT) or in combination with 4-month androgen deprivation (flutamide + triptorelin starting 2 months before radiotherapy, group AD-RT). Lymphadenectomy was mandatory when the risk of node involvement was > 10% (Partin). The primary endpoint was survival without clinical / biochemical relapse at 5 years. Secondary endpoints included overall survival, toxicity (CTCAE v3) and quality of life (QLQ-C30, PR-25). The a-priori sample size was 450 patients, 225 per arm (0.90 power to detect an increase from 75 to 85%, bilateral $\alpha = 0.05$). **Results:** 377 pts were included between September 2003 and June 2010. The inclusions were prematurely closed, due to slow accrual. Intent-to-treat analysis was made for 370 pts (191 RT, 179 AD-RT). Prognostic factors were well balanced between the two arms. The median follow-up duration was 84 months (range: 3 to 132). At 5 years, the probabilities of survival without clinical / biochemical relapse were 76% [95% CI: 69% – 81%] and 84% [78% – 89%] in RT and AD-RT groups, respectively ($p = 0.02$). Overall survival probabilities were 94% [90% - 97%] and 93% [88% - 96%] respectively ($p = 0.54$). Cumulative incidence of biochemical failure were 21% [15% – 26%] and 10% [6% – 15%], respectively ($p < 0.01$). The probabilities of being free of grade 3-4 toxicities were 96% and 95% ($p = 0.69$) for digestive tract, 93% and 95% ($p = 0.44$) for urinary tract. **Conclusions:** 4 months of androgen blockade improves event-free survival at 5 years in pts with intermediate risk prostate adenocarcinoma when treated with high dose radiotherapy. Longer follow-up is required to demonstrate an impact on overall survival.

19. Preliminary results for the advanced salivary gland carcinoma cohort of the phase 1b KEYNOTE-028 study of pembrolizumab.

Author(s): Roger B. Cohen, Jean-Pierre Delord, Toshihiko Doi, Sarina Anne Piha-Paul, Stephen V. Liu, Jill Gilbert, Alain Patrick Algazi, Sara Cresta, Ruey-Long Hong, Christophe Le Tourneau, Daphne Day, Andrea Varga, Elena Elez, John M. Wallmark, Sanatan Saraf, Anne Morosky, Jonathan D. Cheng, Bhumsuk Keam; University of Pennsylvania, Philadelphia, PA; Institut Claudius Regaud, Toulouse, France; National Cancer Center Hospital East, Chiba, Japan; The University of Texas MD Anderson Cancer Center, Houston, TX; Georgetown University Hospital, Washington, DC; Vanderbilt University School of Medicine, Nashville, TN; University of California, San Francisco, San Francisco, CA; Fondazione IRCCS Istituto Nazionale dei Tumori Medical Oncology, Milan, Italy; National Taiwan University Hospital, Taipei, Taiwan; Institut Curie, Paris, France; Princess Margaret Cancer Centre, Toronto, ON, Canada; Gustave Roussy, Villejuif, France; Vall d'Hebron Institute of Oncology, Barcelona, Spain; Maryland Oncology Hematology PA, Rockville, MD; Merck & Co., Inc., Kenilworth, NJ; Seoul National University Hospital, Seoul, Korea, The Republic of

Background: Patients (pts) with treatment-refractory salivary gland cancer have limited treatment options. The PD-1 pathway is upregulated in many tumors leading to immune response suppression. Pembrolizumab (pembro), an anti-PD-1 antibody, blocks interaction between PD-1 and PD-L1 and PD-L2. The nonrandomized KEYNOTE-028 (NCT02054806) trial evaluated the safety and efficacy of pembro in 20 advanced solid tumor cohorts. Results from the salivary gland carcinoma cohort are presented. **Methods:** Key inclusion criteria included advanced (unresectable and/or metastatic) salivary gland carcinoma excluding sarcomas and mesenchymal tumors, failure of systemic therapy, ECOG PS 0-1, and PD-L1 expression in $\geq 1\%$ of tumor or stroma cells by IHC. Pts received pembro 10 mg/kg every 2 wk for up to 24 mo or until confirmed progression, intolerable toxicity, death or withdrawal of consent. Response assessed every 8 wk for the first 6 mo and every 12 wk thereafter. The primary end point was ORR per RECIST v1.1 by investigator review. **Results:** As of Dec 10, 2015, 26 pts were enrolled in this cohort. Median age was 57.0 y; 88.5% were male; 73.1% had an ECOG PS of 1; 73.1% had received prior therapy for metastatic disease. At data cutoff, median follow-up duration was 61.9 wk (range, 8.7-88.4). Treatment-related adverse events (TRAEs) occurred in 22 (84.6%) pts; TRAEs in $\geq 15\%$ of pts were diarrhea (n = 4), decreased appetite (n = 4), pruritus (n = 4), and fatigue (n = 8). 3 (11.5%) pts had grade 3-5 TRAEs which resulted in 1 death (interstitial lung disease); 2 (7.7%) pts discontinued pembro because of a TRAE (grade 2 arthritis; grade 3 hepatitis). Confirmed ORR was 11.5% (PR, n = 3; 95% CI, 2.4-30.2); median duration of response was 17.0 wk (range, 15.1-53.4+). Pts achieving PR had adenocarcinoma (n = 2) and high-grade serous carcinoma (n = 1). Stable disease rate was 46.2% (n = 12; 95% CI, 26.6-66.6). The 6-mo OS rate was 70.4%; the 6-mo PFS rate was 20.7%. At data cutoff, 2 pts were on treatment. **Conclusions:** In this heavily pretreated population, pembro showed promising antitumor activity. Clinical benefit of pembrolizumab in advanced salivary gland carcinoma will be further investigated in the phase 2 KEYNOTE-158 trial (NCT02628067).

20. Improved sarcoma management in a national network of reference centers: Analysis of the NetSarc network on 13,454 patients treated between 2010 and 2014.

Author(s): Jean-Yves Blay, Axel Le Cesne, Nicolas Penel, Emmanuelle Bompas, Florence Duffaud, **Christine Chevreau**, Maria Rios, Pierre Kerbrat, Didier Cupissol, Philippe Anract, Jean-Emmanuel Kurtz, Celeste Lebbe, Nicolas Isambert, Francois Bertucci, Antoine Thyss, Sophie Piperno-Neumann, Pascale Dubray-Longeras, Francoise Ducimetiere, Jean-Michel Coindre, Antoine Italiano; Universite Claude Bernard & Centre Léon Bérard, Lyon, France; Gustave Roussy Cancer Campus, Villejuif, France; Centre Oscar Lambret, Lille, France; Department of Medical Oncology, Centre René Gauducheau, Nantes St. Herblain, France; La Timone University Hospital, Marseilles, France; Institut Claudius Regaud, Toulouse, France; Centre Alexis Vautrin, Vandoeuvre-lès-Nancy, France; Medical Oncology Eugene Marquis Comprehensive Cancer Center, Rennes, France; Centre Val d'Aurelle, Montpellier, France; Hopital Cochin Saint Vincent de Paul, Paris, France; Hôpitaux Universitaires de Strasbourg, Strasbourg, France; Dermatology Department, Saint Louis Hospital, Paris, France; Centre Georges François Leclerc, Dijon, France; Institut Paoli Calmettes, Marseille, France; Centre Antoine-Lacassagne, Nice, France; Institut Curie, Paris, France; Centre Jean Perrin/ERTICa EA 4677, Clermont-Ferrand, France; Centre Léon Bérard, Lyon, France; Institut Bergonié, Department of Pathology, Bordeaux, France; Institut Bergonié, Department of Medical Oncology, Bordeaux, France

Background: Since 2009 a network of 26 reference multidisciplinary centers aiming to improve the quality of care for sarcoma patients (pts) in France was granted by the French National Cancer Institute. We report here on the results of this network on patient management after 5 years. **Methods:** Data of the NetSarc network database include pts characteristics, previous treatment and diagnosis procedures, medical decision, survival and progression. From Jan 2010 to Dec 2014, 13454 newly diagnosed pts were included, soft tissue and visceral representing 10427 (77%) and 3027 (23%) respectively. These represent an estimated 78% of sarcoma case in France in 5 years. Individual Netsarc centers managed a median of 325 (range 39-1529) pts in 5

years. **Results:** 6955 women (52%) and 6499 men (48%), with a median age of 60y (range 0-101) were included. Soft tissue and visceral represented 10427 (77%) and 3027 (23%) pts respectively. LMS (12%), GIST (8.2%), DDLPS (7.3%) and UPS (11%) were the most frequent histotypes. 12% pts had metastases at diagnosis. Between 2010 and 2015, the proportion of pts reviewed in Netsarc reference centers prior to surgery increased from 41% to 48%. A higher number of pts managed in Netsarc centers had proper imaging of the primary tumor prior to surgery (86% vs 59%, $p<0.0001$), and had biopsy prior the first resection (80% vs 36%, $p<0.0001$). 10265 (76%) pts had a surgery, 4304 (42%) within the Netsarc network and 4639 (45%) outside the network, and unknown in 1322 (13%) pts). Patients whose primary surgery was performed in Netsarc centers had R0, R1, R2, and R (unknown or non evaluable) surgery in 49%, 27%, 7%, 16% vs 24%, 31%, 21%, 23% in centers outside Netsarc ($p<0.000001$). 865 (19%) pts had secondary resection after primary surgery in non NetSarc centers vs 252 (6%) in NetSARC centers ($p<0.0001$). Progression free survival (PFS) was better in patients managed in Netsarc reference centers ($p=0.0008$). **Conclusions:** Sarcoma pts managed in reference centers have a significantly higher rate of management according to CPGs, R0 surgery, less reoperations, and better PFS. The number of patients managed prior to surgery in reference centers increases slightly overtime.

21. Phase 1 dose-escalation study of BI 836909, an anti-BCMA bi-specific T-cell engager, in relapsed and/or refractory multiple myeloma (RRMM).

Author(s): Max S. Topp, Michel Attal, Christian Langer, Philippe Moreau, Thierry Facon, Johannes Düll, Benjamin Hebraud, Carlos Gomez-Roca, Gerd Michael Munzert, Edith Gracien, Gerhard Zugmaier, Hermann Einsele; Medizinische Klinik und Poliklinik II, Universitätsklinikum Würzburg, Würzburg, Germany; IUCT-Oncopole, Toulouse, France; University Hospital Ulm, Ulm, Germany; CHU Hôtel Dieu, Nantes, France; CHRU Lille - Hôpital Claude Huriez, Lille, France; Boehringer Ingelheim Pharma GmbH, Ingelheim, Germany; Amgen GmbH, Munich, Germany

Background: Myeloma is an incurable disease that typically follows a relapsing course, with many patients (pts) requiring multiple lines of therapy. Outcomes in RRMM remain poor, particularly after failure of proteasome inhibitor (PI)- and/or immunomodulatory drug (IMiD)-based treatment. There remains a need for novel, targeted therapies for RRMM. BI 836909, a bi-specific T-cell engager (BiTE) that binds CD3 ϵ on T-cells and BCMA on plasma cells, has demonstrated anti-myeloma activity in preclinical models (Hipp et al. ASH 2015; abs 2999). Here we report the design and objectives of the first in-human trial of BI 836909 – a multicenter, open-label, two-part, Phase 1, dose-escalation study evaluating intravenous (IV) and subcutaneous (SC) formulations of BI 836909 in RRMM. **Methods:** Adult pts with RRMM after ≥ 2 prior lines of therapy (including a PI and IMiD) and ECOG PS ≤ 2 are eligible. In part A, pts will receive escalating doses (modified 3+3 design) of BI 836909 as a continuous IV infusion for 4 weeks in 6-week cycles. Dose escalation will proceed based on clinical findings observed during the first 2–4 weeks of cycle 1. Pts will receive up to 5 cycles of treatment (up to 10 cycles for ongoing clinical benefit, at the investigator's discretion) in the absence of disease progression, unacceptable toxicity, or other reasons necessitating withdrawal. Initiation of part B to assess SC BI 836909 will be based on clinical data from part A with the IV formulation. In part B, pts will receive escalating doses (3+3 design) of BI 836909 as a daily SC injection for 4 weeks in 6-week cycles, with stopping criteria as in part A. The primary objective of parts A and B is to determine the maximum tolerated dose of BI 836909 IV/SC for subsequent expansion cohorts. Secondary objectives include evaluation of safety (adverse events; effect on QTcF; immunogenicity), pharmacokinetics, efficacy, pharmacodynamics, and determination of recommended Phase 2 doses. As of 25 January 2016, 9 pts have enrolled in part A. The first four dose cohorts were safe and well tolerated. The study is expected to recruit approximately 100–120 pts in total

22. Ewing sarcoma Family of Tumors in Older Patients (EFyTOP): Management and outcome of Ewing sarcoma family of tumors (EFTs) in patients older than 50 years.

Author(s): Pauline Rochefort, Antoine Italiano, Valerie Laurence, Nicolas Penel, Audrey Lardy-Cleaud, Olivier Mir, **Christine Chevreau**, Francois Bertucci, Emmanuelle Bompas, Loic Chaigneau, Dominique Levy, Thomas Ryckewaert, Sarah Naomie Dumont, Pierre Meeus, Dominique Ranchere, Jean-Yves Blay, Philippe Alexandre Cassier; Centre Léon Bérard, Lyon, France; Institut Bergonié, Department of Medical Oncology, Bordeaux, France; Oncology Department, Institut Curie, Paris, France; Centre Oscar Lambret, Lille, France; Gustave Roussy, Villejuif, France; Institut Claudius Regaud, Toulouse, France; Institut Paoli Calmettes, Marseille, France; Department of Medical Oncology, Centre René Gauducheau, Nantes St. Herblain, France; Institut Regional du Cancer en Franche-Comté - University Hospital, Besançon, France; Institute Curie, Paris, France; University of Miami Sylvester Cancer Center, Miami, FL; Institut d'Hematologie et d'Oncologie Pédiatrique, Lyon, France; Université Claude Bernard & Centre Léon Bérard, Lyon, France

Background: Ewing's sarcoma family of tumors is a group of rare and aggressive tumors. Data on tumor, clinical presentation and treatment in patients (pts) older than 50 years are limited. Outcomes of older pts with EFTs have been reported to be worse than in pediatric population in some studies but with discordant results. **Methods:** We conducted a retrospective analysis among centers of affiliated with the French Sarcoma Group (GSF-GETO) focusing on pts diagnosed with EFTs at age ≥ 50 between 2000 and 2012. Clinical features, treatment modality and outcomes were recorded and analyzed. **Results:** 77 pts were identified. There were 36 females (47%) and the median age at diagnosis was 56 years (range: 50-86). The primary tumor was located in the soft tissue in 59 pts (76.6%) and in the bone in 18 (23.4%). 56 pts (72.8%) had localized disease whereas 21 (27.2%) presented with metastases at diagnosis. Median follow-up was 71 months (m) and median overall survival (OS) was 92.8 m for the whole cohort. Among 56 pts with localized disease, 50 (87.7%) received chemotherapy (CT) in addition to local therapy (surgery in 19 pts, surgery and RT in 37 pts and RT only in 7 pts), and among these, CT was considered intensive in 36 pts (63%). For patients with localized disease, the estimated 3-year OS and relapse free survival (RFS) rates were respectively 73.3% and 62.2%. Recurrence occurred in 43 pts, with a median time to recurrence of 18.2 m. Recurrences were most often metastatic only (62.7%), followed by local only (23%). Recurrence site was lung for 16 pts (37.2%) and bone for 9 pts (20.9%). Median post-recurrence survival was 9.5 m. In univariate analysis only high LDH were marginally associated with worse overall survival in patient with localized disease. All pts with metastatic disease at presentation received CT, their estimated 3-year OS rate was 37%. **Conclusions:** EFTs characteristics in patients ≥ 50 years differ from the pediatric population: they had more likely soft tissue primary tumor and metastatic disease. The outcomes were worse than in younger pts but could be partially explained by less intensive therapy. The management of Ewing sarcoma in adult pts remains to be defined.

23. Regorafenib (RE) in liposarcomas (LIPO), leiomyosarcomas (LMS), synovial sarcomas (SYN), and other types of soft-tissue sarcomas (OTS): Results of an international, double-blind, randomized, placebo (PL) controlled phase II trial.

Author(s): Nicolas Penel, Olivier Mir, Antoine Italiano, Jean-Yves Blay, Jennifer Wallet, Francois Bertucci, **Christine Chevreau**, Sophie Piperno-Neumann, Emmanuelle Bompas, Sebastien Salas, Christophe Perrin, Corinne Delcambre, Bernadette Lieg-Atzwanger, Maud Toulmonde, Thomas Ryckewaert, Isabelle Laure Ray-Coquard, Stephanie Clisant Delaine, Axel Le Cesne, Thomas Brodowicz, Sarcoma Platform Austria and French Sarcoma Group; Centre Oscar Lambret, Lille, France; Gustave Roussy Cancer Campus, Department of Medical

Oncology, Villejuif, France; Institut Bergonié, Department of Medical Oncology, Bordeaux, France; Université Claude Bernard & Centre Léon Bérard, Lyon, France; Institut Paoli Calmettes, Marseille, France; Institut Claudius Regaud, Toulouse, France; Institut Curie, Paris, France; Department of Medical Oncology, Centre René Gauducheau, Nantes St. Herblain, France; Hôpital de la Timone, Marseille, France; Centre Eugène Marquis, Rennes, France; Centre François Baclesse, Caen, France; Graz Medical University, Graz, Austria; Centre Léon Bérard, Lyon, France; Gustave Roussy Cancer Campus, Villejuif, France; Medical University of Vienna, Vienna, Austria

Background: We investigated the activity and safety of RE in doxorubicin-pretreated metastatic soft tissue sarcomas (STS). **Methods:** REGOSARC (NCT01900743) consisted of 4 independent cohorts of patients (pts) who were randomized (1:1) to receive either RE (160 mg/d, 21/28 d) or PL, with optional cross-over. Key-eligibility criteria were age ≥ 18 , metastatic sarcoma, ≤ 3 previous lines of treatment for metastatic sarcoma. The primary endpoint was progression-free survival (PFS) with blinded central radiological review. Statistical assumptions were PFS = 1.6 months (mo) with PL, PFS = 4.6 mo with RE, 1-sided $\alpha = 0.1$ and $\beta = 0.05$ (0.2 in SYN cohort). **Results:** From July 2013 to December 2014, 181 pts previously exposed to doxorubicin (178, 98%), ifosfamide (107, 59%), trabectedin (70, 38%), and pazopanib (6, 3%) were enrolled (89 with RE and 92 with PL; including 70 cross-over). Activity endpoints are displayed in the Table below. Four partial responses have been confirmed in RE arms, one in SYN pts and three in OTH pts (2 angiosarcomas and 1 solitary fibrous tumour). The drug-related maximal toxicity grade distribution by patient with RE (n=89) and PL (n=92) was Grade 5 (1 vs. 0; 1% vs. 0%; hepatitis), Grade 4 (3 vs. 0; 3% vs. 0%), Grade 3 (51 vs. 8; 57 vs. 9%), Grade 2 (18 vs. 22; 20 vs. 24%) and Grade 1 (7 vs. 13; 8 vs. 14%). The most common AEs in RE-treated pts were: asthenia (58, 63%), diarrhea (39, 44%), mucositis (39, 44%), Hand-Foot skin syndrome (39, 44%), anorexia (34, 38%) and arterial hypertension (32, 36%). **Conclusions:** Excluding LIPO, RE is an active drug providing statistically and clinically significant PFS improvement in pre-treated STS pts. Safety of RE is as expected.

24. Resistances to vismodegibs in a French case series of 207 patients with locally advanced basal cell carcinoma.

Author(s): Nicole Basset-Seguin, Hayley Sharpe, Nicolas Poulalhon, Laurent Mortier, Philippe Saiag, Sandrine Monestier, Jeannie Hou, Martine Bagot, Bernard Guillot, Caroline Robert, Nicolas Meyer, Amir Khammari, Florent Grange, Caroline Dutriaux, Brigitte Dréno, Fred De Sauvage; Department of Dermatology, Saint Louis Hospital, 75010, France; Genentech, Inc., South San Francisco, CA; Hospices Civils De Lyon, Pierre Benite, France; Université Lille, Centre Hospitalier Régional Universitaire de Lille, Lille, France; Hôpital Ambroise Paré, Boulogne Billancourt, France; Dermatology and Skin Cancers Department, UMR911 CRO2 Hôpital Timone, Aix-Marseille University, Marseille, France; Hôpital Saint Louis, Paris, France; CHU Montpellier, Montpellier, France; Gustave Roussy Cancer Campus and Paris-Sud University, Villejuif, France; Institut Universitaire du Cancer, Toulouse, France; Dermato-Cancerology department, Nantes University Hospital, Nantes, France; Reims University Hospital, Reims, France; Hôpital Saint-André, CHU Bordeaux, Bordeaux, France; Nantes University, Nantes, France

Background: A Hh pathway inhibitor, vismodegib (VISMO) is approved for the treatment of locally advanced (la BCC) and metastatic BCC (mBCC). While most patients respond to drug treatment, in this work, we studied the frequency of primary resistance (RI), secondary resistance (RII) and stable disease (S) in patients treated with VISMO for laBCC. **Methods:** RI is tumor progression after at least 6 months of treatment, RII is tumor regrowth on treatment after a clear initial response and S is a tumor that has not progressed or responded after 6 months of treatment. The data from patients treated with VISMO were collected in 10 French centers. Demographics, Gorlin's syndrome (GS), treatment history (previous radiotherapy RXT or chemotherapy CHT) and duration of treatment until tumor regrowth were collected. **Results:** 207 patients were analyzed. 10 cases of RI (4.8%), 18 cases of RII (8.7%) and 19 cases of stable disease (9.2%) were observed. Among the RI cases, 3/10 patients had GS, 3/10 previously received RXT, and 2/10 were treated by CHT. Among the RII cases, 3/18 had GS, 1/18 was previously treated by RXT and 1/18 by CHT. The mean time to progression after initiation with VISMO was

13 months (range 6 -24 months). 3/19 S patients had GS, none were previously CHT-treated, but 6/19 had received RXT prior to VISMOM treatment. The molecular exploration of the mechanisms of resistance in these tumors is in progress. We recently showed specific SMO mutations in RII patients, interfering with the ability of vismodegib to inhibit its signaling activity **Conclusions:** Resistance (RI, RII and S) to VISMOM in BCC is low compared with other targeted therapies. The GS context and previous CHT do not seem to influence the incidence of resistance. Established RII mechanisms include mutations in SMO, while the underlying mechanisms of RI and S are still under investigation.

25. Factors influencing HER2 positivity in breast cancer according to statistical modeling and data mining techniques based on a real-world national database: HER-France.

Author(s): Marie-Pierre Chenard, Eric Anger, Marie-Helene Bizollon, Jerome Chetritt, Francesco Bruno Cutuli, Jean Kapfer, Magali Lacroix, Catherine Lefebvre, Eve Lefort, Gaetan mac Grogan, Julien Palasse, Thomas Petit, Bruno Poulet, Vincent Rouleau, Emmanuel Watkin, Dominique Fetique, David Pau, Jean-Pierre Bellocq; Département de Pathologie, Hôpital de Hautepierre, Hôpitaux Universitaires de Strasbourg, Strasbourg, France; Cabinet de Pathologie, Alençon, France; Cabinet de Pathologie, Chalon Sur Saone, France; Institut d'Histo-Pathologie, Nantes, France; Polyclinique De Courlancy, Reims, France; CCAP, Saran, France; Gustave Roussy, Villejuif, France; HISTOSUD, Le Pontet, France; Cabinet Tolbiac, Paris, France; Institut Bergonié, Bordeaux, France; Lab pathologie, Toulouse, France; Centre de pathologie, Amiens, France; Institut de Pathologie de Paris, Malakoff, France; Centre de Pathologie, Perpignan, France; Cy-Path, Lyon, France; AFAQAP, Strasbourg, France; Roche, Neuilly-sur-Seine, France; AFAQAP et Hôpitaux Universitaires de Strasbourg, Strasbourg, France

26. Pembrolizumab in patients with advanced cervical squamous cell cancer: Preliminary results from the phase Ib KEYNOTE-028 study.

Author(s): Jean-Sebastien Frenel, Christophe Le Tourneau, Bert H. O'Neil, Patrick Alexander Ott, Sarina Anne Piha-Paul, Carlos Alberto Gomez-Roca, Emilie Van Brummelen, Hope S. Rugo, Shari Thomas, Sanatan Saraf, Mei Chen, Andrea Varga; Institut de Cancerologie de l'Ouest, Centre René Gauducheau, Saint-Herblain, France; Institut Curie, Paris, France; Indiana University, Simon Cancer Center, Indianapolis, IN; Dana-Farber Cancer Institute, Boston, MA; The University of Texas MD Anderson Cancer Center, Houston, TX; Institut Claudius Regaud, Toulouse, France; The Netherlands Cancer Institute, Amsterdam, Netherlands; University of California, San Francisco, San Francisco, CA; Merck & Co., Inc., Kenilworth, NJ; Gustave Roussy, Villejuif, France

Immunothérapie, cancer cervical à cellules squameuses

Background: Median survival is limited to only ~7 months in patients (pts) with metastatic or recurrent cervical cancer despite current treatments. Upregulation of the PD-1/PD-L1 pathway on tumor or infiltrating immune cells may negatively regulate immunity and contribute to disease progression. Pembrolizumab, an anti-PD-1 antibody, blocks the interaction between PD-1 and its ligands, PD-L1/PD-L2. Results from the cervical cancer cohort of KEYNOTE-028 (NCT02054806), a phase 1b study to evaluate the safety and efficacy of pembrolizumab in pts with advanced solid tumors, are presented. **Methods:** Key eligibility criteria included advanced cervical squamous cell cancer, failure of prior systemic therapy, ECOG PS 0-1, and PD-L1 expression in $\geq 1\%$ of tumor or stroma cells by IHC. Pembrolizumab 10 mg/kg was given every 2 wk for up to 24 mo or until confirmed progression, intolerable toxicity, death, or withdrawal of consent. Response was assessed every 8 wk for the first 6 mo and

every 12 wk thereafter. The primary end point was ORR per RECIST v1.1 by investigator assessment. **Results:** 24 pts with advanced cervical cancer were enrolled; median age was 41.5 y, 75.0% had an ECOG PS of 1, and 62.5% had received ≥ 2 prior therapies for metastatic disease. As of Dec 10, 2015, median follow-up duration was 48.9 wk (range, 5.6-90 wk). 18 (75.0%) pts experienced a treatment-related adverse event (TRAE), with pyrexia (n = 4) and rash (n = 3) occurring in $\geq 10\%$ of pts. 5 (20.8%) pts had grade 3 TRAEs, 2 of whom discontinued pembrolizumab (colitis, Guillain-Barre syndrome). No grade 4 or 5 TRAEs occurred. ORR (confirmed) was 12.5% (3/24; 95% CI, 2.7%-32.4%; all were PRs); the median duration of response was 19.3 wk (range, 17.7-52.0 wk). The stable disease (SD) rate was 12.5% (3/24; 95% CI, 2.7%-32.4%); the median duration of SD was 19.6 wk (range, 16.3-29.7+ wk). The 6-mo PFS rate was 13.0%; the 6-mo OS rate was 66.7%. **Conclusions:** Pembrolizumab was well tolerated and showed promising antitumor activity in pts with PD-L1⁺ advanced cervical squamous cell cancer. The clinical benefit of pembrolizumab in advanced cervical cancer will be further investigated in the phase 2 KEYNOTE-158 trial (NCT02628067).

27. Relations between clinical outcomes and pharmacokinetics of irinotecan, oxaliplatin, and 5-fluorouracil during hepatic artery chronomodulated delivery of intravenous cetuximab in patients with extensive liver metastases from colorectal cancer: A translational study in European trial OPTILIV.

Author(s): Francis Levi, Abdoulaye KarabouÃ©, Marie-Christine Etienne-Grimaldi, Gilles Paintaud, C. N. J. Focan, Pasquale F. Innominato, Mohamed Bouchahda, Gerard Milano, Etienne Chatelut, ARTBC International, Chronotherapy Group; HÃ´pital Paul Brousse, Villejuif, France; AK-SCIENCE, Vitry Sur Seine, France; Antoine Lacassagne Center, Nice, France; Universite FranÃ§ois-Rabelais de Tours, CNRS, GICC UMR 7292, CHRU de Tours, Service de Pharmacologie-Toxicologie, Tours, France; Department of Oncology, Centre Hospitalier ChrÃ©tien, Clinique Saint-Joseph, Liege, Belgium; Warwick Medical School, Coventry, United Kingdom; Medical Oncology Department, INSERM U935, Paul Brousse Hospital, Villejuif, France; Laboratory of Oncopharmacology, Antoine Lacassagne Center, Nice, France; Institut Claudius Regaud, IUCT, Ã©quipe n°14, UniversitÃ© Paul Sabatier, Toulouse, France

Background: The combination of hepatic artery infusion (HAI) of irinotecan, 5-fluorouracil and oxaliplatin (IFO) with iv cetuximab (Cet) achieved prolonged survival in colorectal cancer patients (pts) with extensive liver metastases (LM-CRC) despite prior chemotherapy (LÃ©vi et al. Ann Oncol 2016). Systemic drug and metabolite exposure is unknown during the HAI delivery of combination chemotherapy in patients with extensive liver metastases. **Methods:** We estimated the plasma pharmacokinetics of IFO and their main metabolites during the first course of chronomodulated triplet HAI, and related them to toxicity (CTC-AE grades) and efficacy. **Results:** 11 patients, 7 males, 4 females, aged 33 to 72 years, had PS = 0, one to three prior intravenous chemotherapy protocols, a median number of 7 liver metastases, involving a median number of 7 liver segments. Maximal concentration (C_{max}) and area under the curve (AUC) for all drugs and metabolites were not related to response, progression-free survival and overall survival. In contrast, consistent associations were found between the AUC of irinotecan, SN38, total oxaliplatin and platinum ultrafiltrate (P-UF), and leukopenia grade after first course (Spearman test, $|r| > 0.50$; $0.05 < p < 0.08$). Moreover, P-UF C_{max} and AUC significantly predicted for the grades of diarrhea ($|r| = 0.82$, $p = 0.004$ and $|r| = 0.73$, $p = 0.017$, respectively), and anemia ($|r| = 0.87$, $p = 0.001$ and $|r| = 0.78$, $p = 0.008$, respectively). AUCs and/or C_{max} of the HAI drugs and/or their main metabolites displayed consistent relations with leukopenia, anemia, diarrhea, but also fatigue and anorexia over the initial 3 courses as well. **Conclusions:** Hematologic and intestinal toxicities of this new highly effective protocol mostly related to the systemic exposure of the three HAI drugs. In contrast, the high antitumor efficacy involves the direct drug exposure of liver metastases. Mathematical modelling will help personalize HAI combination chronotherapy for jointly enhancing efficacy and reducing toxicity.

28. Mature results of the GETUG 13 phase III trial in poor-prognosis germ-cell tumors (GCT).

Author(s): Karim Fizazi, Aude Flechon, Gwenael / Le Teuff, Jozef Mardiak, Lance C. Pagliaro, Lionnel Geoffrois, Pierre Kerbrat, **Christine Chevreau**, Remy Delva, Frederic Rolland, Christine Theodore, Guilhem Roubaud, Gwenaelle Gravis, Jean-Christophe Eymard, Jean-pierre Malhaire, Claude Linassier, Muriel Habibian, Maria Reckova, Christopher Logothetis, Stephane Culine; Institut Gustave Roussy, University of Paris Sud, Villejuif, France; Centre Léon Bérard, Lyon, France; Gustave Roussy, Villejuif, France; Department of Clinical Oncology, National Cancer Institute, Comenius University, Bratislava, Slovakia; The University of Texas MD Anderson Cancer Center, Houston, TX; Centre Alexis Vautrin, Vandoeuvre-Lès-Nancy, France; Medical Oncology Eugene Marquis Comprehensive Cancer Center, Rennes, France; Institut Claudius Regaud, Toulouse, France; Institut de Cancérologie de l'Ouest, Angers, France; Centre René Gauducheau, Saint-Herblain, France; Hospital Foch, Suresnes, France; Department of Medical Oncology, Institut Bergonie, Bordeaux, France; Medical Oncology, Institut Paoli Calmette, Hôpital de Jour, Marseille, France; Institut Jean-Godinot, Reims, France; Centre Hospitalo-Universitaire, Brest, France; Oncologie Medicale, Tours, France; UNICANCER, Paris, France; POKO Poprad, Poprad, Slovak Republic; Department of Medical Oncology, Hopital Saint-Louis, Paris, France

Background: Until 2014, standard treatment for poor-prognosis GCT was 4 BEP plus surgery and cure was achieved in only 50% of patients (pts) (IGCCCG 1997). The tumor marker decline rate identified pts with a better outcome (J Clin Oncol 2004, 22: 3868-76). The GETUG 13 phase III trial established that switching pts with an unfavorable decline to intensified chemotherapy results in improved progression-free survival (PFS) (Lancet Oncol 2014; 15: 1442-50). We assessed the long-term efficacy and toxicity in pts treated in GETUG 13. **Methods:** 263 pts with IGCCCG poor-prognosis GCT were treated with 1 BEP. hCG and AFP were assessed at day 21: 1) 51pts with a favorable decline continued BEP (Fav-BEP); 2) 203 pts with an unfavorable decline were randomized to receive either BEP (Unfav-BEP) or a dose-dense regimen (Unfav-dose-dense), consisting of paclitaxel-BEP plus oxaliplatin x 2 cycles, followed by 2 cycles of cisplatin, ifosfamide, and bleomycin + G-CSF. PFS and overall survival (OS) (logrank) and long-term toxicity (NCI-CTC criteria) were assessed. **Results:** The median follow-up is 5.6 years (range 0.3; 11.9). The 5-year PFS rate is 60% in the Unfav-dose-dense arm vs 47% in the Unfav-BEP arm (HR: 0.65 [0.43-0.97]; p=0.037). The 5-year OS rate is 70.4% and 60.8%, respectively (HR: 0.69 [0.43-1.11]; p=0.12). Side effects evolved favorably, with 3 pts in the Unfav-dose-dense arm reporting grade 3 motor neurotoxicity at 1 year but no reported toxicity \geq grade 2 after year 2. The prognostic value of the tumor marker decline was confirmed: 70% vs 47% for 5-year PFS (p=0.006), and 78% vs 61% for OS (p=0.02). Salvage high-dose chemotherapy plus a stem cell transplant was implemented in 8% in the Unfav-dose-dense arm and 17% in the Unfav-BEP arm (p=0.035). **Conclusions:** With a mature follow-up, GETUG 13 shows that pts with poor-prognosis GCT and an unfavorable tumor marker decline after 1 BEP who are treated with intensified chemotherapy achieve significantly improved PFS, numerically better OS, minimal long-term toxicity, and a reduced need for high-dose salvage chemotherapy plus a stem cell transplant. These data support integrating this strategy as a standard of care for these rare pts.

29. Molecular targeted therapies (MTT) in advanced chordoma (AC) patients (pts).

Author(s): Loic Lebellec, Axel Le Cesne, Nicolas Penel, Jean-Yves Blay, **Christine Chevreau**, Emmanuelle Bompas, Francois Bertucci, Didier Cupissol, Michel Fabbro, Esma Saada, Florence Duffaud, Loic Feuvret, Alice Bonneville-Levard, Jacques-Olivier Bay, Elodie Vauleon, Georges Noel, Bruno Chauffert, Olivier Mir, French Sarcoma Group and ANOCEF; Centre Oscar Lambret, Lille, France; Gustave Roussy Cancer Campus, Villejuif,

France; Université Claude Bernard & Centre Léon Bérard, Lyon, France; Institut Claudius Regaud, Toulouse, France; Department of Medical Oncology, Centre René Gauducheau, Nantes St. Herblain, France; Institut Paoli Calmettes, Marseille, France; Department of Medical Oncology, Centre Val d'Aurelle Paul Lamarque, Montpellier, France; ICM Val d'Aurelle, Montpellier, France; Ceutie Antoine Lacassagne, Nice, France; La Timone University Hospital, Marseilles, France; APHP, Paris, France; Centre Léon Bérard, Lyon, France; Cellular Therapy and Clinic Hematology Unit for Adults, CHU Clermont-Ferrand, France; Eugène Marquis Cancer Institute, Rennes, France; Radiotherapy, Centre P. Strauss, Strasbourg, France; University Hospital (CHU) - Department of Medical Oncology, Amiens, France; Gustave Roussy Cancer Campus, Department of Medical Oncology, Villejuif, France

Background: The data about the clinical benefit of MTT in AC pts are sparse. **Methods:** Retrospective study of 74 AC pts treated between January 2004 and August 2015 in 12 major French sarcoma or neuro-oncology centers. **Results:** The sex ratio M/F was 42/32. The median age was 59 (12-86). The primary sites were sacrum (51, 69%), mobile spine (7, 9%) and skull base (16, 22%). Previous treatments were surgery (52, 70%), radiotherapy (36, 49%) and chemotherapy (10, 14%). Metastases present in 27 pts (37%) included lung (16, 22%), liver (4, 6%) and other sites (14, 19%). The 1st line of MTT consisted in imatinib (58, 78%), sorafenib (11, 15%), erlotinib (3, 4%), sunitinib and temsirolimus (1 each, 3%). The best objective response was PR (3, 4%: 2 with imatinib and 1 with sorafenib), SD (55, 74%), PD (9, 12%) and NE (7, 9%). Symptomatic improvement (SI) was seen in 23/61 assessable pts (38%) and was associated with SD/PR ($p = 0.007$). The PFS was 9 mo and the OS was 59 mo. In univariate analysis, the sole prognostic factor for PFS was prior radiotherapy (6 vs 14 mo, $p = 0.031$). Prognostic factor for OS were: age as continual variable ($p = 0.001$), WHO-PS (not reached, 47, 66, 4 respectively with 0, 1, 2 and 3, $p = 0.026$), primary location (sacrum 65 mo, mobile spine 49 mo and skull base 16 mo, $p = 0.0001$), pain requiring morphine (34 vs 65, $p = 0.051$), prior radiotherapy (30 vs 65 mo, $p = 0.004$), presence of liver met. (6 vs 59 mo, $p = 0.015$), presence of other met. (22 vs 59, $p = 0.022$) and anemia (34 vs 88, $p = 0.043$). The multivariate Cox model retained three independent prognostic factors: sacral primary location (HR = 0.22, $p = 0.043$), pain requiring morphine (HR = 3.6, $p = 0.006$) and liver met. (HR = 7.5, $p = 0.002$). 37 pts (50%) have received a 2nd line MTT, including imatinib (15, 41%), sorafenib (7, 19%) and erlotinib (6, 16%). The PFS was 5 mo; 2 PR (5%) were seen with erlotinib. SI with 2nd line ($n = 7$, 20%) was associated with SI in 1st line ($p = 0.000037$). SD/PR seen with 1st line were not predictive of SD/PR in 2nd line ($p = 0.95$). 18 pts have received 3rd line, including imatinib (3, 16%), sorafenib (8, 44%). The PFS was 2 mo; SI was seen in 5 pts (27%) and 1 pt (5%) receiving sorafenib experienced PR. **Conclusions:** Larger databases are needed to confirm the clinical benefit and validate clinical predictive factors

30. Overall survival in patients with advanced melanoma (MEL) who discontinued treatment with nivolumab (NIVO) plus ipilimumab (IPI) due to toxicity in a phase II trial (CheckMate 069).

Author(s): F. Stephen Hodi, Michael Andrew Postow, Jason Alan Chesney, Anna C. Pavlick, Caroline Robert, Kenneth F. Grossmann, David F. McDermott, Gerald P Linette, **Nicolas Meyer**, Jeffrey K. Giguere, Sanjiv Agarwala, Montaser F. Shaheen, Marc S. Ernstoff, David R. Minor, April K. Salama, Matthew H. Taylor, Patrick Alexander Ott, Joel Jiang, Paul Gagnier, Jedd D. Wolchok; Dana-Farber Cancer Institute, Boston, MA; Memorial Sloan Kettering Cancer Center, New York, NY; University of Louisville, Louisville, KY; NYU Perlmutter Cancer Center, New York, NY; Institute Gustave Roussy, Villejuif-Paris-Sud, France; Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; Beth Israel Deaconess Medical Center, Boston, MA; Washington University, St. Louis, MO; Institut Universitaire du Cancer, Toulouse, France; Greenville Health System, Seneca, SC; St Luke's Cancer Center and Temple University, Bethlehem, PA; University of New Mexico Cancer Center, Albuquerque, NM; Cleveland Clinic, Cleveland, OH; California Pacific Center for Melanoma Research, San Francisco, CA; Duke University, Durham, NC; Oregon Health & Science University, Portland, OR; Bristol-Myers Squibb, Princeton, NJ

Background: Results from CheckMate 069 demonstrated a significant improvement in objective response rate (ORR) and progression-free survival (PFS) with NIVO+IPI vs IPI alone in treatment-naïve patients (pts) with *BRAF* wild-type MEL (*N Engl J Med* 2015;372:2006). We evaluated overall survival (OS) in pts who discontinued treatment due to toxicity in this study. **Methods:** Pts (N = 142) were randomized 2:1 to receive NIVO 1 mg/kg plus IPI 3 mg/kg or IPI 3 mg/kg plus placebo every 3 weeks x 4 doses, followed by NIVO 3 mg/kg or placebo, respectively, every 2 weeks until disease progression or unacceptable toxicity. The primary endpoint was ORR in pts with *BRAF* wild-type tumors. Secondary and exploratory endpoints included PFS and OS. A post-hoc analysis was performed to evaluate OS in pts who discontinued treatment due to toxicity. **Results:** At a follow-up of ≥18 months, median OS in pts who discontinued treatment was not reached with NIVO+IPI and was 11.2 months for IPI alone (Table). Similar 18-month OS rates were observed in pts who discontinued NIVO+IPI due to toxicity and in the overall treatment group (Table). Among pts who discontinued NIVO+IPI, ORR was 68% (27% achieved a complete response). Median duration of response was not reached and 21 of 30 pts (70%) remain in response. Grade 3/4 treatment-related adverse events (AEs) occurred in 55% of pts in the NIVO+IPI group vs 22% with IPI, and led to discontinuation in 30% and 9% of pts, respectively. In pts who discontinued NIVO+IPI due to toxicity, resolution rates of treatment-related select AEs ranged from 89% to 100% (40% for endocrine AEs). Efficacy updates, including 2-year OS rates, will be presented for these pts. **Conclusions:** These data suggest that pts who discontinue NIVO+IPI treatment due to drug toxicity derive an OS benefit similar to that observed in the overall population.

31. Checking HER2 rates in breast cancer: A 4 year-experience with a nationwide database containing 105,717 records—HER-France.

Author(s): Marie-Pierre Chenard, Eric Anger, Marie-Helene Bizollon, Jerome Chetritt, Jean Kapfer, Magali Lacroix, Catherine Lefebvre, Eve Lefort, Elisabeth Luporsi-Gely, Gaetan mac Grogan, Julien Palasse, Thomas Petit, Bruno Poulet, Vincent Rouleau, Emmanuel Watkin, Caroline Egele, Jean-Pierre Bellocq; Département de Pathologie, Hôpital de Hautepierre, Hôpitaux Universitaires de Strasbourg, Strasbourg, France; Cabinet de Pathologie, Alençon, France; Cabinet de Pathologie, Chalon Sur Saone, France; Institut d'Histo-Pathologie, Nantes, France; CCAP, Saran, France; Gustave Roussy, Villejuif, France; HISTOSUD, Le Pontet, France; Cabinet Tolbiac, Paris, France; ICL Alexis Vautrin, Vandoeuvre-Lès-Nancy, France; Institut Bergonié, Bordeaux, France; Lab pathologie, Toulouse, France; Centre de pathologie, Amiens, France; Institut de Pathologie de Paris, Malakoff, France; Centre de Pathologie, Perpignan, France; Cy-Path, Lyon, France; AFAQAP, Strasbourg, France; AFAQAP et Hôpitaux Universitaires de Strasbourg, Strasbourg, France