

IUCT Rangueil-Larrey et Purpan

8 Présentations Posters

Afatinib in patients with metastatic *HER2*-mutant lung cancers: An international multicenter study.

Sub-category:

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

Category:

Lung Cancer—Non-Small Cell Metastatic

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

9071

Poster Board Number:

Poster Session (Board #397)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 9071)

Author(s): Wei-Chu Victoria Lai, Louisiane Lebas, Julie Milia, Tristan Alexandra Barnes, Oliver Gautschi, Solange Peters, Roberto Ferrara, Ai Ni, Joshua K. Sabari, Stephen John Clarke, Nick Pavlakis, Charles M. Rudin, Maria E. Arcila, Natasha B. Leighl, Frances A. Shepherd, Mark G. Kris, Julien Mazieres, Bob T. Li; Memorial Sloan Kettering Cancer Center, New York, NY; [Toulouse University Hospital, Toulouse, France](#); Hôpital Larrey Centre Hospitalier Universitaire Toulouse, Toulouse, France; Princess Margaret Cancer Centre, Toronto, ON, Canada; Cantonal Hospital Lucerne, Luzern, Switzerland; Lausanne University Hospital, Lausanne, Switzerland; University of Verona, Verona, Italy; Memorial Sloan-Kettering Cancer Center, New York, NY; Northern Cancer Institute, University of Sydney, Sydney, Australia

[Abstract Disclosures](#)

Abstract:

Background: Human epidermal growth factor 2 (*HER2*, *ERBB2*) mutations have been identified as oncogenic drivers in 3% of lung cancers. Afatinib is an irreversible tyrosine kinase inhibitor of HER1 (EGFR), HER2 and HER4 and has been described in case reports to have activity in *HER2*-mutant lung cancers. However, there is little data to inform the clinical use of afatinib. **Methods:** We reviewed patients with metastatic *HER2*-mutant lung cancers treated with afatinib among 7 institutions between 2009 and 2016. The primary endpoint was investigator assessed overall response rate using RECIST v1.1. Other data collected included types of *HER2* mutations, duration of afatinib treatment and overall survival. **Results:** We identified 27 patients with metastatic *HER2*-mutant lung cancers treated with afatinib. Median age at diagnosis was 63 (range 40 to 84); majority were men (n = 16; 59%) and never-smokers (n = 18; 67%). All tumors were adenocarcinomas, and the majority were Stage IV at initial diagnosis (n = 16; 59%). A 12-base pair (bp) in-frame insertion YVMA in exon 20 (p.A775_G776insYVMA) was present in 16 patients (59%). In addition, there were three 9-bp insertions, two 3-bp insertions and two single bp substitutions (L755F and D769H) in exon 20; two single bp substitutions (S310F) in exon 8; one exon 17 V659E mutation; and one single-nucleotide polymorphism (Ile655Val). Median duration on afatinib was 2 months (range 1 to 27); median line of prior treatment was 3 (range 1 to 6). Eight patients had previously received trastuzumab prior to afatinib and one concurrently with afatinib. Overall response rate was 15% (n = 4; 95% CI 4 to 34%); the four partial responses lasted 5, 5, 6 and 10 months. The 3 longest partial responders had a 12-bp insertion in exon 20 (YVMA); the remaining partial responder had a 9-bp insertion in exon 20. Median overall survival from diagnosis date of metastatic disease was 23 months (95% CI 18 to 62). **Conclusions:** Afatinib produced partial responses in 15% of patients with metastatic *HER2*-mutant lung cancers, including insertion YVMA. Our findings confirm the activity of afatinib and provide data supporting a framework for its use in the care of patients with *HER2*-mutant lung cancers.

Second- or third-line nivolumab (Nivo) versus nivo plus ipilimumab (Ipi) in malignant pleural mesothelioma (MPM) patients: Results of the IFCT-1501 MAPS2 randomized phase II trial.

Sub-category:

[Mesothelioma](#)

Category:

Lung Cancer—Non-Small Cell Local-Regional/Small Cell/Other Thoracic Cancers

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

LBA8507

Citation:

J Clin Oncol 35, 2017 (suppl; abstr LBA8507)

Author(s): Arnaud Scherpereel, [Julien Mazieres](#), Laurent Greillier, Pascal Dô, Olivier Bylicki, Isabelle Monnet, Romain Corre, Clarisse Audigier-Valette, Myriam Locatelli-Sanchez, Olivier Molinier, Luc Thiberville, Thierry Urban, Catherine Ligeza-poisson, David Planchard, Elodie Amour, Franck Morin, Denis Moro-Sibilot, Gerard Zalcman, French Cooperative Thoracic Intergroup (IFCT); University Hospital of Lille, Lille, France; [Hôpital Larrey Centre Hospitalier Universitaire Toulouse, Toulouse, France](#); Assistance Publique - Hopitaux De Marseille, Marseille, France; CLCC Baclesse, Caen, France; HIA Percy, Clamart, France; CHI of Creteil, Creteil, France; Rennes University Hospital, Rennes, France; Pneumology Department, Centre Hospitalier Toulon Sainte-Musse, Toulon, France; HCL Lyon-Sud, Pierre-Bénite, France; Le Mans Regional Hospital, Le Mans, France; Centre Hospitalier Unversitaire Rouen, Rouen, France; CHU Angers University, Angers, France; Clinique Mutualiste de l'Estuaire, Saint-Nazaire, France; Gustave Roussy, Villejuif, France; IFCT, Paris, France; Intergroupe Francophone de Cancérologie Thoracique, Paris, France; IFCT, Chu de Grenoble, Grenoble, France; GH Bichat Claude Bernard, Paris, France

[Abstract Disclosures](#)

Abstract:

The full, final text of this abstract will be posted online at 7:30 a.m. (ET) on Monday, June 5.

IFCT-GFPC-1101 trial: A multicenter phase III assessing a maintenance strategy determined by response to induction chemotherapy compared to continuation maintenance with pemetrexed in patients (pts) with advanced non-squamous (NSQ) NSCLC.

Sub-category:

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

Category:

Lung Cancer—Non-Small Cell Metastatic

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

9003

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 9003)

Author(s): Maurice Perol, Clarisse Audigier-Valette, Olivier Molinier, Alexis B. Cortot, Jacques Margery, Lionel Moreau, Virginie Westeel, Pascal Dô, Fabrice Barlesi, Eric Pichon, Gerard Zalcman, Patrick Dumont, Nicolas Girard, Michel Poudenx, [Julien Mazieres](#), Jacques Cadranet, Didier Debieuvre, Jérôme Dauba, Denis Moro-Sibilot, Pierre Jean Souquet, French Cooperative Thoracic Intergroup (IFCT); Department of Thoracic Oncology, Centre Léon Bérard, Lyon, France; Pneumology Department, Centre Hospitalier Toulon Sainte-Musse, Toulon, France; Le Mans Regional Hospital, Le Mans, France; Centre Hospitalier Regional Universitaire Lille, Lille, France; HIA Percy, Clamart, France; Centre Hospitalier Pneumologie Colmar, Colmar, France; University of Franche-Comté, Besancon, France; CLCC Baclesse, Caen, France; Aix-Marseille University, Assistance Publique Hopitaux de Marseille, Marseille, France; Centre Hospitalier Universitaire Tours, Tours, France; Centre Hospitalier Universitaire de Caen, Caen, France; Centre Hospitalier De Chauny - Service de Pneumologie, Chauny, France; Louis Pradel Hospices Civils de Lyon, Lyon, France; CLCC Lacassagne, Nice, France; [Hôpital Larrey Centre Hospitalier Universitaire Toulouse, Toulouse, France](#); Hôpital Tenon, AP-HP and Faculté de Médecine Pierre et Marie Curie, Université Paris VI, Paris, France; Emile Muller Hospital, Mulhouse, France; Department of Gastroenterology, Hopital Layne, Mont De Marsan, France; IFCT, Chu de Grenoble, Grenoble, France; Hopital Lyon-Sud, Pierre-Bénite, France

[Abstract Disclosures](#)

Abstract:

Background: Benefit coming from maintenance treatment appears greater for switch maintenance in pts with disease stabilization (SD) while it might be larger for continuation maintenance in pts with objective response (OR). This study assessed a maintenance strategy conditioned by response to cisplatin-gemcitabine (CG): continuation maintenance with G for pts with OR and switch maintenance with pemetrexed (P) for pts with SD compared with a control arm using P continuation maintenance following cisplatin-pemetrexed (CP) induction regimen. **Methods:** Eligibility criteria included age 18-70 years, PS of 0-1, untreated stage IV NSQ NSCLC without EGFR mutation or ALK rearrangement, ineligibility to bevacizumab. Pts were randomized 1:1 to receive either experimental CG arm: CG (4 cycles) followed by G maintenance in case of OR followed by second-line P or switch maintenance with P for pts with SD, or standard CP arm: 4 cycles CP induction regimen followed by

maintenance P. Overall survival (OS) was the primary endpoint; secondary endpoints included PFS, response rate and safety. **Results:** Between Jul 2012 and Jun 2016, 932 pts were randomized (CG: 467, CP: 465). Pts characteristics were balanced between the arms. 255 pts (54.6%) in the CG arm received maintenance treatment (G: 142, P: 113) while 274 pts (58.9%) received P maintenance in the CP arm. Median number of maintenance cycles was 5 for G and 4 for P in both arms. The OS adjusted HR was 0.97 (95% CI 0.84, 1.13; $p=0.72$); median OS: 10.9m CG vs. 10.4m CP. The HR for PFS was 0.96 (95% CI 0.84, 1.10; $p=0.56$); median PFS: 5.0m CG vs. 4.7m CP. Safety profile was as expected during induction chemotherapy. During maintenance, grade ≥ 3 hematological AEs occurred in 28% and 31% of pts in CG and CP, respectively, with febrile neutropenia (2.4% vs. 1.1%), anemia (9.4% vs. 11.7%), thrombocytopenia (6.7% vs. 5.8%). No grade ≥ 3 non-hematological AEs occurred in $>5\%$ of pts except for asthenia (3.9% CG vs. 5.1% CP). **Conclusions:** Adapting maintenance strategy according to response to induction chemotherapy does not improve patient outcome. Clinical trial information: [NCT01631136](https://clinicaltrials.gov/ct2/show/study/NCT01631136)

Mature overall survival (OS) results from the LUME-Meso study of nintedanib (N) + pemetrexed/cisplatin (PEM/CIS) vs placebo (P) + PEM/CIS in chemo-naïve patients (pts) with malignant pleural mesothelioma (MPM).

Sub-category:

[Mesothelioma](#)

Category:

Lung Cancer—Non-Small Cell Local-Regional/Small Cell/Other Thoracic Cancers

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

8506

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 8506)

Author(s): Anna K. Nowak, Federica Grosso, Nicola Steele, Silvia Novello, Sanjay Papat, Laurent Greillier, Tom John, Natasha B. Leighl, Martin Reck, Nick Pavlakis, Jens Benn Soerensen, David Planchard, Giovanni Luca Ceresoli, Brett Gordon Maxwell Hughes, [Julien Mazieres](#), Mark A. Socinski, Derek Velema, Ute von Wangenheim, Nassim Morsli, Giorgio V. Scagliotti; School of Medicine, Faculty of Medicine and Health Sciences, University of Western Australia, Crawley, Australia; Oncology, SS Antonio e Biagio General Hospital, Alessandria, Italy; Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; University of Turin, Department of Oncology, Torino, Italy; Royal Marsden Hospital, London, United Kingdom; Assistance Publique - Hopitaux De Marseille, Marseille, France; Olivia Newton-John Cancer Research Institute, Heidelberg, Australia; Princess Margaret Cancer Centre, Toronto, ON, Canada; Department of Thoracic Oncology, Lung Clinic Grosshansdorf, Member of the German Center for Lung Research (DZL), Grosshansdorf, Germany; Northern Cancer Institute, University of Sydney, Sydney, Australia; Rigshospitalet Blegdamsvej 9, Copenhagen, Denmark; Gustave Roussy, Department of Medical Oncology, Villejuif, France; Cliniche Humanitas Gavazzeni, Department of Oncology, Bergamo, Italy; The Prince Charles Hospital, Brisbane, Australia; [HOP Larrey, Onco, Chemin de Pouvoirville, Toulouse, France](#); University of Pittsburgh Centre Avenue, Pittsburgh, PA; Boehringer Ingelheim Canada Ltd./Ltée, Burlington, ON, Canada; Boehringer Ingelheim Pharma GmbH and Co. KG, Biberach, Germany; Boehringer Ingelheim France, S.A.S., Paris, France; University of Turin, Department of Oncology, S. Luigi Hospital, Torino, Italy

[Abstract Disclosures](#)

Abstract:

Background: LUME-Meso is a Phase (Ph) II/III, double-blind, randomized study. N targets MPM by inhibiting VEGFR 1–3, PDGFR α/β , FGFR 1–3, Src and Abl kinases. Primary analysis of the Ph II data demonstrated improved progression-free survival (PFS; hazard ratio [HR]=0.56; 95% confidence interval [CI] 0.34–0.91; $p=0.017$). Mature Ph 2 OS and updated PFS results are reported here. **Methods:** Pts with unresectable MPM (ECOG PS 0–1) were stratified by histology (epithelioid/biphasic) and randomized 1:1 to receive ≤ 6 cycles PEM (500 mg/m²)/CIS (75 mg/m²) Day 1 + N or P (200 mg bid, Days 2–21), followed by N or P monotherapy until progression or toxicity. The primary endpoint was PFS. The primary OS analysis and updated PFS analysis were performed as predefined. **Results:** 87 pts were randomly assigned (N=44, P=43). OS benefit favored N over P treatment (HR=0.77; 95% CI 0.46–1.29; $p=0.319$; 62 [71%] OS events) and was greatest in epithelioid pts (HR=0.70; 95% CI 0.40–1.21; $p=0.197$) with a median (m) OS gain of 5.4 months (mOS [95% CI]: 20.6 [16.2–28.8] N vs 15.2 [12.2–23.6] P). Updated PFS results (HR=0.54; 95% CI 0.33–0.87; $p=0.010$) also showed greatest benefit for epithelioid pts (HR=0.49; 95% CI 0.30–0.82; $p=0.006$) with a mPFS gain of 4.0 months (mPFS [95% CI]: 9.7 [7.2–12.4] N vs 5.7 [5.5–7.0] P). Improved forced vital capacity, objective response rates and duration of response were also observed with N treatment. Drug-related adverse events (AEs) in N- vs P-treated pts were 97.7% vs 97.6%. Grade ≥ 3 AEs of note included neutropenia (27.3% vs 4.9%), ALT (11.4% vs 0) and GGT (6.8% vs 0) elevations, and diarrhea (6.8% vs 0). AEs led to trial discontinuation in only 3 (6.8%) N vs 7 (17.1%) P pts. **Conclusions:** Mature Ph II OS data show that adding N to standard 1st-line treatment gives a strong signal towards improved OS. Updated PFS confirmed the primary analysis; AEs were manageable. The greatest clinical benefit was observed in pts with epithelioid histology. Median survival of 20.6 months in epithelioid pts

treated with N is unprecedented in advanced MPM trials. Ph III is actively recruiting in this pt population. Clinical trial information: [NCT01907100](#)

Updated survival of patients (pts) with previously treated *BRAF* V600E–mutant advanced non-small cell lung cancer (NSCLC) who received dabrafenib (D) or D + trametinib (T) in the phase II BRF113928 study.

Sub-category:

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

Category:

Lung Cancer—Non-Small Cell Metastatic

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

9075

Poster Board Number:

Poster Session (Board #401)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 9075)

Author(s): David Planchard, Benjamin Besse, Tae Min Kim, Elisabeth A. Quoix, Pierre Jean Souquet, [Julien Mazieres](#), Fabrice Barlesi, Harry J.M. Groen, Egbert F. Smit, Christina S. Baik, Byoung Chul Cho, Ronan Joseph Kelly, Mark A. Socinski, Silvia Novello, James R. Rigas, Vanessa Giannone, Anthony Michael D'amelio, Pingkuan Zhang, Bijoyesh Mookerjee, Bruce E. Johnson; Gustave Roussy, Villejuif, France; Seoul National University Hospital, Seoul, Republic of Korea; University Hospital of Strasbourg, Strasbourg, France; Hopital Lyon-Sud, Pierre-Bénite, France; [Rangueil-Larrey Hospital, Paul Sabatier University, Toulouse, France](#); Aix-Marseille University, Assistance Publique Hopitaux de Marseille, Marseille, France; University of Groningen, University Medical Center Groningen, Groningen, Netherlands; Vrije Universiteit VU Medical Centre, Amsterdam, Netherlands; University of Washington, Seattle, WA; Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD; University of Pittsburgh, Pittsburgh, PA; Department of Oncology, University of Turin, Turin, Italy; Geisel School of Medicine at Dartmouth, Hanover, NH; Novartis Pharmaceuticals Corporation, East Hanover, NJ; Dana-Farber Cancer Institute, Boston, MA

[Abstract Disclosures](#)

Abstract:

Background: *BRAF* V600E mutations occur in 1% to 2% of lung adenocarcinomas and act as oncogenic drivers. Initial cohorts of the BRF113928 (NCT01336634) trial evaluated efficacy and safety of D monotherapy (cohort A; n = 78) or D + T (cohort B; n = 57) in pts with previously treated *BRAF*V600E–mutant metastatic NSCLC. At primary analysis, overall response rates (ORRs) were 33.3% and 63.2% in pts who received D or D + T, respectively. Furthermore, durable response (median duration of response [DOR], 9.0 mo) was observed in D + T pts. Here, we present an updated survival analysis based on additional follow-up. **Methods:** In this phase 2 trial, 2 cohorts (A and B) of pts with previously treated metastatic *BRAF*V600E–mutant NSCLC were enrolled sequentially. The primary endpoint was investigator-assessed ORR. Secondary efficacy endpoints included progression-free survival (PFS), DOR, and overall survival (OS). D and T were dosed orally at the established phase 2 dose of D 150 mg twice daily and T 2 mg once daily. **Results:** This updated analysis had a median follow-up of 16.2 mo, which represented an additional 10 mo of follow-up. Median OS was 12.7 mo (95% CI, 7.3-16.3) with 57 deaths reported for pts treated with D monotherapy and 18.2 mo (95% CI, 14.3-not estimable [NE]) with 33 deaths reported for pts treated with D + T. Detailed efficacy results are presented in the table. Investigator-assessed ORR, DOR, and PFS were supported by independent review committee assessments. No new safety signals were observed for D + T. **Conclusions:** This update of the BRF113928 study confirms that durable responses and encouraging survival were achieved with combination D + T in pts with *BRAF*V600E–mutant NSCLC. Clinical trial information: [NCT01336634](#)

	D (n = 78)	D + T (n = 57)
ORR, n (%)^a	25 (32.1) ^b	38 (66.7)
95% CI	21.9-43.6	52.9-78.6
DOR, median, mo^a	9.6 ^b	9.8
95% CI	5.4-15.2	6.9-16.0
PFS, median, mo^a	5.5 ^b	10.2
95% CI	2.8-7.3	6.9-16.7
12-mo PFS, %	26	43
95% CI	15.9-36.6	29.8-55.7
24-mo PFS, %	14	22
95% CI	7.2-24.1	11.4-35.6
OS, median, mo	12.7	18.2
95% CI	7.3-16.3	14.3-NE
12-mo OS, %	52	66
95% CI	39.7-62.3	52.4-77.1
24-mo OS, %	31	39
95% CI	20.8-42.0	25.5-52.1

^aInvestigator assessment. ^bData cutoff, November 21, 2014.

Vitamin K epoxide reductase complex subunit 1 (VKORC1): A pharmacogenomic predictor of response and survival in patients (pts) on triplet hepatic artery infusion (HAI) and intravenous cetuximab (IV-Cet) for initially unresectable liver metastases from colorectal cancer (uLM-CRC) (EU trial OPTILIV).

Sub-category:

[Pharmacology](#)

Category:

Developmental Therapeutics—Clinical Pharmacology and Experimental Therapeutics

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

2569

Poster Board Number:

Poster Session (Board #61)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 2569)

Author(s): Francis Levi, Raphael Saffroy, Abdoulaye Karaboue, Christophe Desterke, Valerie Boige, Mohamed Hebbar, Denis Michel Smith, Mohamed Bouchahda, Pasquale Innominato, Julien Taieb, Carlos Carvalho, **Rosine Guimbaud**, C. N. J. Focan, Michel Ducreux, Rene Adam, Antoinette Lemoine; Cancer Chronotherapy Unit, Warwick Medical School, Coventry, United Kingdom; Hopital Paul Brousse Biochemistry Department, University Paris-Sud, Villejuif, France; AK-SCIENCE, Vitry Sur Seine, France; Universite Paris Sud 11 UMS33 INSERM Unit, Villejuif, France; Service d'Oncologie Digestive, Gustave Roussy, Villejuif, France; University Hospital, Marcq En Baroeul, France; Medical Oncology, Bordeaux University Hospital, Bordeaux, France; Paul Brousse Hospital, Oncology Department, Villejuif, French Southern Territories; University of Warwick, Medical School, Coventry, United Kingdom; Georges Pompidou European Hospital, Paris, France; Champalimaud Clinical Centre, Lisbon, Portugal; **University Hospital of Rangueil, Toulouse, France**; Department of Oncology, Centre Hospitalier Chrétien, Clinique Saint-Joseph, Liege, Belgium; Institut Gustave Roussy, Service d'Oncologie Digestive, Villejuif,

France; Centre Hépatobiliaire, AP-HP, Hôpital Paul Brousse, Villejuif, France; Paul Brousse Hospital, Villejuif, France

Abstract Disclosures

Abstract:

Background: The HAI of Irinotecan-Oxaliplatin-5-Fluorouracil (IFO) with IV-Cet achieved 29.7% complete uLM-CRC resections (R0+R1) and an overall median survival (OS) of 25.7 months in previously treated pts (*Lévi, Ann Oncol 2016*). **Methods:** To identify pharmacogenomic predictors of outcomes, 207 single nucleotide polymorphisms (SNPs) from 34 pharmacology genes were analysed in blood mononuclear cells (ADME PGx, MassArray platform, Sequenom, USA). Relations between SNPs and tumor response, R0+R1, survival, and toxicities were tested using adjusted Mann Whitney, Fisher Exact, Log Rank tests and Hardy-Weinberg Equilibrium. **Results:** Pts (16F;36M; 33-76 yo; WHO performance status 0-1) received protocol treatment as 2nd (21 pts) or 3-4thline (31 pts). VKORC1 SNPs in promoter (rs9923231) and intron (rs9934438) were consistently associated with early and objective responses, and overall survival. For rs9923231, T/T (N = 8) as compared to C/T (N = 21) had greatest chance of achieving early response (50% vs 5%, p = 0.029) or 4-y survival (46% vs 0%, p = 0.006). VKORC1 SNPs also related to HA thrombosis (rs992331, T/T, 77% vs C/C, 30%, p = 0.04). In contrast, NAT2 SNPs (rs1041983 and rs1801280) were associated with up to 5-fold differences in R0-R1 resection rate. Statistically significant associations (p < 0.05) of SNPs with clinical outcomes were found for oxydo-reduction (CYP2E1 and HA thrombosis; CYP2C9 and diarrhea; CYP2C19 and diarrhea, fatigue, and early response), conjugation (UGT1A1 and diarrhea; NAT2 and fatigue); and transport (ABCB1 or SLC0B3 and neutropenia; SLC22A1 and diarrhea; SLC 15A2 and early response). **Conclusions:** VKORC1 was highlighted for the first time, as a pharmacogenomic predictor of HAI efficacy for LM-CRC. Conversion-to-resection was associated with NAT2 polymorphism. VKORC1 γ -carboxylates vitamin K-dependent proteins. Its polymorphism guides personalized warfarin dosing. VKORC1 SNPs determination could help identify the uLM-CRC pts who best benefit from intensive HAI therapy. Clinical trial information: [NCT00852228](https://clinicaltrials.gov/ct2/show/study/NCT00852228)

Single-agent dose-finding cohort of a phase 1/2 study of lenvatinib (LEN) in children and adolescents with refractory or relapsed solid tumors.

Sub-category:

[Pediatric Solid Tumors](#)

Category:

Pediatric Oncology

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

10544

Poster Board Number:

Poster Session (Board #301)

Citation:

J Clin Oncol 35, 2017 (suppl; abstr 10544)

Author(s): Nathalie Gaspar, Maria Soledad Gallego Melcon, Rajkumar Venkatramani, Stefan S. Bielack, Michela Casanova, Franco Locatelli, Estelle Thebaud, Charlotte Rigaud, Samuel Abbou, [Marion Gambart](#), Bruce Morland, Isabelle Aerts, Silvija Kraljevic, Di Li, Hina Maniar, Seiichi Hayato, Corina E Dutcus, Quentin Campbell Hewson; Institut Gustave Roussy, Villejuif, France; University Hospital Vall d'Hebron, Barcelona, Spain; Texas Children's Hospital, Houston, TX; Klinikum Stuttgart Olgahospital, Stuttgart Cancer Center, Stuttgart, Germany; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Bambino Gesù Children's Hospital, Rome; University of Pavia, Pavia, Italy; CHU Nantes and UMR892 INSERM, Nantes, France; [Children's Hospital, CHU, Toulouse, France](#); Birmingham Children's Hospital, Birmingham, United Kingdom; Institut Curie, Paris, France; Eisai Co., Ltd., Hatfield, United Kingdom; Eisai Co., Ltd., Woodcliff Lake, NJ; Eisai Co., Ltd., Tokyo, Japan; North of England Principal Treatment Centre for Cancer in Children and Young People, Great North Children's Hospital, Newcastle-upon-Tyne, United Kingdom

Abstract Disclosures

Abstract:

Background: LEN is an inhibitor of vascular endothelial growth factor (VEGF) receptors 1–3, fibroblast growth factor receptors 1–4, platelet-derived growth factor receptor α , RET, and KIT. LEN is approved in adults for radioiodine-refractory differentiated thyroid cancer (DTC) and in combination with everolimus in patients (pts) with advanced renal cell carcinoma. We show results from the single-agent LEN dose-finding part of a phase 1/2 study in children and adolescents with solid tumors. **Methods:** Pts had any relapsed or refractory solid tumor, evaluable or measurable disease, were aged 2 to ≤ 18 years, had < 2 prior VEGF-targeted therapies, and adequate organ function. A starting dose of LEN 11 mg/m² was escalated with a time-to-event continual reassessment method. The primary endpoint was to determine the LEN recommended dose (RD). Secondary objectives included best overall response (BOR), objective response rate, safety, and pharmacokinetics (PK). **Results:** 23 pts enrolled (11 mg/m²: n = 5, 14 mg/m²: n = 11, 17 mg/m²: n = 7). The most common tumors were rhabdomyosarcoma (n = 5),

Ewing sarcoma (n = 4), and neuroblastoma (n = 3). 3 Dose-limiting toxicities occurred in cycle 1 at 14 mg/m² (increased alanine aminotransferase: 1; hypertension: 2). All pts had any-grade treatment-emergent adverse events (TEAEs; grade 3/4: 65%). Most common any-grade TEAEs were vomiting (52%), abdominal pain (48%), decreased appetite (48%), diarrhea (44%), and hypothyroidism (44%). 1 Pt discontinued LEN due to a LEN-related TEAE (hypertension). BOR was stable disease (n = 10). Effect of age on oral clearance and central volume of distribution was not significant. Exposure was similar to that in adults. LEN 14 mg/m²/day was therefore identified as the RD. Updated cohort 1 data will be shown. **Conclusions:** The LEN RD in children and adolescents was similar to the adult dose and showed a reasonable safety profile. PK in these pts did not differ significantly from that in adults. The phase 1b dose-finding study of LEN in combination with chemotherapy in osteosarcoma (OS) and phase 2 LEN monotherapy (RD 14 mg/m²) parts in DTC and OS are ongoing. Clinical trial information: [NCT02432274](#)

A phase IIb of eryaspase in combination with gemcitabine or FOLFOX as second-line therapy in patients with metastatic pancreatic adenocarcinoma (NCT02195180).

Sub-category:

[Pancreatic Cancer](#)

Category:

Gastrointestinal (Noncolorectal) Cancer

Meeting:

[2017 ASCO Annual Meeting](#)

Abstract No:

e15718

Citation:

J Clin Oncol 35, 2017 (suppl; abstr e15718)

Author(s): Pascal Hammel, Jean-Baptiste Bachet, Iman El-Hariry, Fabienne Portales, Laurent Mineur, Jean-Philippe Metges, Christelle De La Fouchardiere, Christophe Louvet, Farid El Hajbi, Roger Faroux, [Rosine Guimbaud](#), David Tougeron, Julien Volet, Thierry Lecomte, Christophe Tournigand, Christine Rebischung, Willy Berlier, Anu Gupta, Jerome Cros, Thierry Andre; Hôpital Beaujon, Paris, France; Hopital Universitaire Pitie-Salpetriere, Paris, France; Erytech Pharma Inc., Lyon, France; Institut du Cancer de Montpellier, Montpellier, France; Institut Sainte-Catherine, Avignon, France; Institut de Cancerologie de l'Ouest, Brest, France; Centre Léon-Bérard, Lyon, France; Institut Mutualiste Montsouris, Paris, France; Centre Oscar Lambret, Lille, France; Centre Hospitalier Departemental Les Oudairies, La Roche-Sur-Yon, France; [University Hospital of Ranguueil, Toulouse, France](#); Gastroenterology Department, Poitiers University Hospital, Poitiers, France; University Hospital of Reims, Reims, France; Hôpital Trousseau, Tours, France; Department of Medical Oncology, Hôpital Mondor, APHP, Créteil, France; Institut Daniel Hollard, Grenoble, France; ERYTECH Pharma, Lyon, France; Erytech Pharma Inc., Cambridge, MA; APHP-INSERM U1149 Universite Paris Diderot, Clichy, France; Medical Oncology Department, Saint-Antoine Hospital, Paris, France

[Abstract Disclosures](#)

Abstract:

Background: L-asparaginase (L-ASP) hydrolyses asparagine (ASN) leading to depletion of this amino acid. While normal cells are protected from ASN requirement due to their ability to produce ASN, leukemic lymphoblasts and most cancer cells have a very low level or even lack of L-asparagine synthetase (ASNS), and thus depend on serum ASN for their proliferation and survival. L-ASP depletes serum ASN, which in turn inhibits the protein synthesis, resulting in cell cycle arrest and apoptosis in susceptible cancer cells, especially pancreatic cancer cells Eryaspase, which is L-ASP encapsulated in red blood cells, recently showed an encouraging activity and improved safety profile compared to L-ASP in patients (pts) with relapsed ALL. Knowing that up to 70% of pancreatic adenocarcinomas (PC) have low or null ASNS expression (Bachet Pancreas 2015), prompted us to evaluate the efficacy and safety of eryaspase in combination with chemo in PC. **Methods:** This open label, multicenter phase II randomized study (2:1) enrolled pts with second-line metastatic PC. Pts eligible to gemcitabine or FOLFOX regimen (according to first line chemo) were randomized to chemo +/- eryaspase (100 IU/Kg D3 and D17 of 4-wk regimen) until disease progression Primary end point: progression free survival in pts with ASNS negative tumors (0/1+). ASNS expression was measured using immunohistochemistry and optical density. Key secondary endpoints: PFS in ASNS positive pts (2+/3+), overall survival, biomarkers (KRASmutation, cell free DNA), and safety. **Results:** 141 pts were enrolled. Treatment was generally well tolerated, with no safety concerns based on IDMC reviews. ASNS expression was negative in 69%, and positive in 31% of the pts At the time of submission, PFS and OS analysis and the correlation of ASNS expression with clinical outcomes were not yet available but will be presented at the meeting. **Conclusions:** This is the largest set of PC pts tested for the expression of ASNS and treated in second line with an asparaginase combined with chemotherapy. The ASNS expression levels may be a potential therapeutic target and therefore predictive of response to eryaspase for the treatment of advanced PC. Clinical trial information: [NCT02195180](#)