LATE PUBLICATION ABSTRACTS
MONDAY, SEPTEMBER 7, 2015

CLINICAL TRIALS 1
MONDAY, SEPTEMBER 7, 2015 - 10:45-12:15

ORAL11.01 Bevacizumab 15mg/kg Plus Cisplatin-Pemetrexed (CP) vs CP in Malignant Pleural Mesothelioma (MPM): IFCT-GFPC-0701 MAPS Randomized Phase 3 Trial Arnaud Scherpereel[1], Julien Mazières[2], Jacques Margery[3], Laurent Greillier[4], Clarisse Audigier-Valette[5], Denis Moro-Sibilot[6], Olivier Molinier[7], Romain Corre[8], Isabelle Monnet[9], Valérie Gounant[10], Frédéric Rivière[11], Henri Janicot[12], Radj Gervais[13], Chrystele Locher[14], Bernard Milleron[15], Quân Tran[15], Marie Paule Lebitasy[15], Christian Creveuil[16], Jean-Jacques Parienti[16], Franck Morin[15], Gérard Zalcman[16] [1]*Pneumology, CHU Lille, Lille/France,* [2]*Hôpital Larrey, Centre Hospitalier Universitaire de Toulouse, Toulouse/France,* [3]*Gustave Roussy, Villejuif/France,* [4]*Hôpital Nord, Marseille/France,* [5]*Chi Toulon, Toulon/France,* [6]*Pôle Thorax Et Vaisseaux, Unité D'Oncologie Thoracique, Service de Pneumologie,, Grenoble/France,* [7]*Ch Le Mans, Le Mans/France,* [8]*CHU, Rennes/France,* [9]*Chi Créteil, Créteil/France,* [10]*Aphp, Cancerest, Tenon University Hospital, Paris/France,* [11]*Hia Percy, Clamart/France,* [12]*CHU, Clermont-Ferrand/France,* [13]*Centre François Baclesse, Caen/France,* [14]*Ch, Meaux/France,* [15]*French Cooperative Thoracic Intergroup (Ifct), Paris/France,* [16]*CHU, Caen/France*

Background: MPM median overall survival (OS) did not exceed 13 months with pemetrexed-platinum doublet, with virtually no surviving patients at 5 years. Vascular endothelial growth factor is a potent mitogen for MPM cells. **Methods:** In this French multicenter randomized phase 3 trial, eligible patients had unresectable, histologically proved MPM, age < 76, no prior chemo, PS 0-2, no thrombosis, nor bleeding. Randomized patients (1:1) received pem 500 mg/m2, CDDP 75 mg/m2 at D1, with (arm B) or without bevacizumab (arm A), 15 mg/kg Q21D, for 6 cycles. Arm B non-progressive patients received bevacizumab maintenance therapy until progression or toxicity. Primary endpoint was OS. 445 patients were to be randomized, and 385 events observed, to show a significant OS improvement, with 80% statistical power, 5% a-risk. **Results:** From Feb. 2008 to Jan. 2014, 448 patients were included in 73 centers. Males: 75.4%, median age: 65.7 years (range 34.7-75.9), PS 0-1: 96.7%. The IDMC recommended a second interim analysis after 85% of events. On 01-Jan-2015, the duration since last news was < 30 days in 105 out of 106 still living patients. Overall survival was significantly longer in the experimental arm (median: 18.8 months, 95%CI[15.9-22.6] vs. 16.1 months, 95%CI[14.0-17.9] for the reference arm, (adj.HR = 0.76, 95%CI[0.61; 0.94], p = 0.012). With only 46/448 non-progressive patients at the date of analysis, median PFS was 9.6 months, 95%CI[8.5-10.6] in bevacizumab arm vs. 7.5 months, 95%CI[6.8-8.1] (adj.HR = 0.62, 95%CI[0.50-0.75], p < 0.0001). G3-4 hematological toxicities did not significantly differ in the two arms (49.5% vs. 47.3%). Significantly more G3 proteinuria (0.0 vs. 3.1%), G3 hypertension (0.0 vs. 23%), G3-4 arterial thrombotic events (0.0 vs. 2.7%) were observed in bevacizumab arm. QOL and exploratory biomarkers studies will be also presented at time of the meeting. **Conclusion:** Bevacizumab addition to pemetrexed/cis-platin provides a significantly longer survival in pts with MPM, with acceptable toxicity, making this triplet a new treatment paradigm. **Keywords:** IFCT, Mesothelioma, bevacizumab, phase III

QUALITY OF LIFE AND TRIALS
MONDAY, SEPTEMBER 7, 2015 - 10:45-12:15

ORAL12.05 Impact of Time to Drug Approval on Potential Years of Life Lost: The Compelling Need for Improved Trial and Regulatory Efficiency David J. Stewart[1], Andrew A. Stewart[2], Paul Wheatley-Price[1], Gerald Batist[3], Hagop Kantarjian[4], Joan Schiller[5], Mark Clemons[1], John-Peter Bradford[6], Laurel Gibbons[7], Razelle Kurzrock[8] [1]*Medicine, University of Ottawa, Ottawa/ON/Canada,* [2]*The Lethal Diseases Help Project, Ottawa/ON/Canada,* [3]*Mcgill University, Montreal/QC/Canada,* [4]*University of Texas MD Anderson Cancer Center, Houston/TX/United States of America,* [5]*Hematology/Oncology, UT Southwestern, Dallas/United States of America,* [6]*Bradford Bachinski Ltd and the Lethal Diseases Help Project, Ottawa/ON/Canada,* [7]*The Ottawa Hospital and the Lethal Diseases Help Project, Ottawa/AB/Canada,* [8]*University of California San Diego, San Diego/CA/United States of America*

Background: Survival of incurable cancer patients is improving gradually. Several hundred new therapies are under development. However, internationally, regulatory complexity slows progress by increasing drug development costs (hence, fewer drugs can be assessed with available resources) and by producing numerous speed bumps that delay approval of useful drugs and that increase resources required to document that other agents are ineffective. **Methods:** We assessed cancer therapies undergoing phase III trials between 2001 and 2015. To be included, trials had to document statistically significant improvement in overall survival. We excluded adjuvant trials and trials in uncommon malignancies. To determine the number of life-years potentially lost per year required for drug approval, we multiplied the improvement in median survival in years by the estimated number of patients (North American and worldwide) dying annually from the relevant malignancy. **Results:** In the Table, we present the life-years lost per year required for approval for 21 therapies in 10 malignancies. When the combined impact of all tumor sites and drugs are considered together, there were 29 life-years lost in North America per hour of delay in therapy approval (1 for every 2 minutes of delay) and 260 life-years lost worldwide per hour of delay (1 for every 14 seconds of delay). These numbers do not take into account impact of drugs non-evaluable due to cross-over or missing survival data, drugs that were prematurely abandoned, drugs still undergoing investigation, or approaches for non-malignant lethal diseases.

Malignancy	Therapy	Median survival gain (yrs)	Life-years lost per year required to achieve drug approval*	
			North America	Worldwide
NSCLC	Erlotinib	0.17	25,344	198,730
NSCLC	Bevacizumab	0.17	25,344	198,730
NSCLC (EGFR-expressing)	Cetuximab	0.10	12,899	101,150
NSCLC (squamous)	Nivolumab	0.27	11,917	93,450
Breast	Eribulin	0.21	9,536	95,485
Breast (HER2+ve)	Trastuzumab	0.40	2,743	27,504
Breast (HER2+ve)	Trastuzumab emtansine	0.48	3,312	33,211
Breast (HER2+ve)	Pertuzumab	1.31	8,969	89,938
Colorectal	Bevacizumab	0.39	23,139	238,610
Colorectal	Oxaliplatin	0.38	22,136	228,263
Colorectal	Regorafinib	0.12	6,906	71,218
Colorectal (EGFR-expressing)	Cetuximab	0.13	7,157	73,805
Gastric (HER2+ve)	Trastuzumab	0.23	605	34,871
Head/Neck	Cetuximab	0.23	1,988	25,920
Prostate	Cabazitaxel	0.20	6,308	51,680
Prostate	Enzalutamide	0.40	12,616	103,360
Prostate	Abiraterone	0.38	12,080	98,967
Prostate	Sipuleucel-T	0.36	11,354	93,024
Renal	Temsirolimus	0.30	4,757	34,800
Renal	Sunitinib	0.38	6,026	44,080
Renal**	Sorafenib	0.29	4,599	33,640
Melanoma	Ipilumumab	0.31	3,382	8,938
Melanoma (BRAF-mutant)	Vemurafenib	0.33	1,785	8,938
Melanoma (BRAF-wildtype)	Nivolumab	0.42	2,284	11,440
Myeloma	Pomalidomide	0.39	4,923	28,860
Myeloma	Bortezomib	1.11	13,985	81,992
Hepatocellular	Sorafenib	0.23	5,290	160,057
Cumulative (all sites)			251,626	2,278,662

* Median survival gain (years) x no. patients dying per year
**Placebo patients censored at time of cross-over

Conclusion: Clearly, the survival gains associated with the foregoing drugs are only modest. Despite this, there would be a large negative impact associated with approval delays even if factors such as co-morbidities, performance status, ability to pay, etc, limit the number of patients treated to a fraction of the total dying from a specific malignancy. There are numerous opportunities to improve efficiency of cancer drug approval without sacrificing safety or data integrity. This requires urgent attention. **Keywords:** regulatory delays, Life-years lost, urgent need for reform

MASCC-IASLC JOINT SESSION: PALLIATIVE AND SUPPORTIVE CARE
TUESDAY, SEPTEMBER 8, 2015 - 16:45-18:15

ORAL29.01 Results From Phase III Trials of Anamorelin in Advanced Non-Small Cell Lung Cancer Patients with Cachexia: ROMANA 1 and 2 Amy Abernethy[1], Kenneth Fearon[2], John Friend[3], Ying Yan[3], Elizabeth Duus[3], David Currow[4] [1]*Durham University, Durham/NC/United States of America,* [2]*Western General Hospital, Edinburgh/United Kingdom,* [3]*Helsinn Therapeutics (Us), Inc., Iselin/NJ/United States of America,* [4]*Flinders University, Adelaide/SA/Australia*

Background: Cachexia is a debilitating condition often observed in patients with advanced non-small cell lung cancer (NSCLC). A decrease in body weight (BW), in particular loss of lean body mass (LBM), is a primary characteristic, and is associated with worsening functional status, quality of life, and survival. Despite the high prevalence and substantial clinical impact of cachexia in patients with advanced cancer, limited therapeutic options exist. Anamorelin is a novel, orally active, selective ghrelin receptor agonist that mimics the appetite-enhancing and anabolic effects of ghrelin. ROMANA 1 and 2 are two randomized, double-blind, Phase III trials evaluating the efficacy and safety of anamorelin in patients with advanced NSCLC and cachexia. **Methods:** In ROMANA 1 (NCT01387269; N=484) and ROMANA 2 (NCT01387282; N=495), patients with unresectable stage III/IV NSCLC and cachexia (≥5% weight loss during prior 6 months or body mass index <20kg/m^2) were randomized (2:1) to anamorelin 100 mg daily or placebo, for 12 weeks. Co-primary endpoints were change in LBM and handgrip strength (HGS) over 12 weeks. Secondary endpoints included change in BW and in the anorexia/cachexia domain of the Functional Assessment of Anorexia/Cachexia Therapy questionnaire over 12 weeks, and pooled 1-year overall survival (OS) from both studies. Exploratory endpoints included summarizing the incidence of patients who maintained/gained LBM from baseline during 12 weeks by treatment group. Post-hoc analysis compared OS data in patients who had decrease in LBM during 12 weeks versus those who maintained/gained LBM. Safety and tolerability of anamorelin were also evaluated. **Results:** Over 12 weeks, anamorelin significantly increased median LBM versus placebo in ROMANA 1 (1.10 vs –0.44 kg; p<0.001) and ROMANA 2 (0.75 vs –0.96 kg; p<0.001); in both studies there was no difference in HGS changes between treatment arms. A significantly greater proportion of patients in the anamorelin arm versus the placebo arm maintained/gained LBM in both ROMANA 1 (58.1% vs 36.9%; p<0.001) and ROMANA 2 (51.5% vs 26.5%; p<0.001). Post-hoc analysis showed that OS was improved for patients who maintained/gained LBM versus patients who lost LBM (HR, 0.53 [95% CI, 0.42, 0.68]; p<0.001). Anamorelin-treated patients also significantly gained BW (2.20 vs 0.14 kg; p<0.001, and 0.95 vs –0.57 kg; p<0.001), and had significantly improved anorexia-cachexia symptoms and concerns (4.12 vs 1.92; <0.001, and 3.48 vs 1.34; p=0.002), compared with placebo-treated patients, in ROMANA 1 and 2, respectively.

The most frequent drug-related adverse event (AE) in the anamorelin arm in both ROMANA 1 and 2 was hyperglycemia (5.3% and 4.2%); there were few drug-related grade ≥3 AEs in the anamorelin arm versus the placebo arm (0.9% vs 1.2% and 2.7% vs 2.5%). **Conclusion:** Anamorelin significantly increased LBM and BW, and improved anorexia-cachexia symptoms and concerns, compared with placebo, in patients with advanced NSCLC and cachexia. Change from baseline in HGS was similar in both treatment arms. A significantly greater proportion of patients maintained/gained LBM in the anamorelin arm versus the placebo arm. When LBM was stable or increased, OS was significantly improved. Anamorelin treatment over 12 weeks was also well tolerated.
Keywords: Cachexia, Anamorelin, ROMANA, Lean body mass