Annals of Oncology

Official Journal of the European Society for
Medical Oncology and the Japanese Society of Medical Oncology
Volume 27, 2016 Supplement 6
Abstract Book of the 41st ESMO Congress (ESMO 2016)
Copenhagen, Denmark, 7–11 October 2016

Institut Universitaire du Cancer -Toulouse- Oncopole **: 7**
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Soit 30 abstracts

Dont 5 communications libres (proffered paper session)
+ 1 clinical practice guidelines

biomarkers

55PD Vemurafenib (VM) in non-melanoma V600 and non-V600 BRAF mutated cancers: first results of the ACSE trial

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Background: BRAF mutations (mut) are observed in several cancer histotypes at low frequency (<5%). VM is active in BRAF mutated melanoma. Recently, non-melanoma BRAF-V600E-mutated cancers were also reported to respond to BRAF inhibitors. The ACSE VM study is the 2nd ACSE program launched by the French National Cancer Institute (INCa). This program aims to avoid off-label use and allows a safe and controlled access to targeted therapies outside their label. Here we report the first results of the ACSE VM study.
Methods: ACSE VM is a phase II trial in patients (pts) with advanced cancers with a BRAF mut identified through the INCa molecular genetic platforms failing standard treatment. Pts with various BRAF V600 mutated cancers (e.g., lung, ovarian, bladder, thyroid, prostate cancers, cholangiocarcinoma (CK), sarcoma/GIST, multiple myeloma, chronic lymphocytic leukemia (CLL) and hairy cell leukemia (HCL)) are included in dedicated cohorts to receive VM 960 mg BID. Pts with non-V600 BRAF mut (exon 11, 15) or other BRAF alteration are also eligible in a specific miscellaneous cohort (misc.). A Bayesian approach allows sequential analyses in each cohort and early stopping using an inefficacy boundary for objective response (OR) rate of 10%. OR is evaluated every 8 weeks using RECIST V1.1 criteria for solid tumors and specific criteria for myeloma, CLL and HCL.
Results: From Oct. 2014 to Apr. 2016, 78 out of 1500+ screened pts were included at 96 centers. Median age was 67 years [18-84], 51% were females. Median duration of treatment was 1.9 months [0.2-11.0]. Most frequent grade ≥3 AEs were skin and gastrointestinal toxicities.
Conclusions: Nationwide screening for BRAF mut enabled rapid inclusion of BRAF mutated patients in this basket trial. Antitumor activity of VMwas important in NSCLC, HCL, and misc. V600 mutated tumors. Non-V600 mutated tumors derived no benefit. Clinical trial identification: NCT02304809
Legal entity responsible for the study: Unicancer, Inca. Funding: Unicancer, Inca, ARC.
Disclosure: J-Y. Blay: Advisory board: Roche, Novartis, Bayer, MSD, Lilly, Pharmamar, Deciphera. corporate-sponsored research: Roche, Novartis, Bayer, MSD, Lilly, Pharmamar. D. Perol: Advisory Board: Roche. F. Barlesi: Board: Pfizer. D. Moro-Sibilot: Consultant: Pfizer, Novartis, Lilly, Boehringer, Astra Zeneca, Amgen, BMS. X. Troussard: Advisory Board: Roche, Janssen, Gilead. S. Leboulleux: Consulting: Genzyme, Sanofi, Astra Zeneca, Roche, Merck. Travel: Genzyme, Sanofi, Bayer. D. Malka: Honoraria: Roche, Amgen, Bayer, Teva, Celgene, Lilly, Merck, Merck Serono, Sanofi-Aventis. Consulting: Roche, Merck. Travel: Roche, Sanofi-Aventis. All other authors have declared no conflicts of interest.

69P External quality assessment of EGFR testing in circulating DNA: a french pilot study

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Background: Tissue testing for NSCLC patients is routinely performed in France in the regional platforms certified by the French National Cancer Institute (INCa). All laboratories participate in an annual EQA scheme for tissue testing, but there is no EQA for circulating tumor DNA testing. Therefore, we set up a pilot study to assess quality testing in western France
Methods: Artificial samples were prepared by supplementing normal plasma (Clinisciences) with DNA extracted from control FFPE sections (Horizon Diagnostics) or plasma from NSCLC patients. Aliquots (2 ml) of 8 different samples were sent in dry ice. DNA extraction and EGFR testing (exon 19 deletions, L858R, G719X and T790M mutations) were performed according to local practice. Data were collected and compared to the expected results.
Results:We collected 10 complete sets of data from 9 labs. DNA was extracted from 1 ml (n = 4) or 2ml (n = 6) using the QIAmp circulating DNA kit (Qiagen; n = 3), the Maxwell system (Promega; n = 4) or the cfDNA sample prep (Roche; n = 3). Mutation testing was performed by NGS (n = 3), using the COBAS EGFRv2 (Roche; n = 3) or the Therascreen EGFR RGQ kit (Qiagen; n = 2), using droplet digital PCR (BioRad; n = 1) or pyrosequencing (Qiagen; n = 1). A single false positive result was observed (T790M detected by NGS). The sensitivity (number of mutations detected / number of mutations present in the set of samples) and the number of correct genotypes are presented on the table. This pilot study suggested that, under the specific conditions of this scheme, the COBAS kit was the most sensitive approach.
Concl**u**sions: This pilot EQA allowed each lab to evaluate its practice and could be used to improve their process. These information will be important for labs that have not yet decided which technique to use for ctDNA testing. Samples were relatively simple to prepare and it will be easy to scale-up this process. A similar approach using other genes (BRAF, KRAS and NRAS) will also be developed. Supported by a grant from Astra Zeneca.
Legal entity responsible for the study: N/A
Funding: Astra Zeneca
Disclosure: M.G. Denis: Advisory board Qiagen. All other authors have declared no conflicts of interest.

92P Impact of Kras mutant subtypes on PD-L1 expression in lung adenocarcinoma

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Background: Clinical responses to immune checkpoint blockade by anti-PD-1/PD-L1 monoclonal antibodies in non-small-cell lung cancer (NSCLC) may be associated with PD-L1 expression. This study was undertaken to determine the expression profile of PD-L1 in patients with Kras-mutant lung adenocarcinoma (LUAD) and to investigate the activation of Kras codon subtypes as a mechanism of PD-L1 regulation Methods: PD-L1 expression was evaluated by IHC (SP142 clone, Ventana) on 117 LUAD (KrasWT, n = 51; Krasmut, n = 66). Stable cell lines were generated by
transfection of Kras-G12D, G12V, G12C and WT plasmids into Beas2B bronchial cells.
Results: IHC analysis showed higher expression of PD-L1 in both tumor and immune cells in Kras-mutant LUAD compared with KrasWT tumors (37% vs. 18%; P = 0.005). Kras-mutant PD-L1+ tumors had increased CD66b+ neutrophil infiltrates and lower CD8+ T-cell content than PD-L1− tumors. In vitro, mutant Kras led to significantly higher cell-surface PD-L1 expression and PD-L1 transcripts, notably in KrasG12C and KrasG12V cells, suggesting PD-L1 transcriptional regulation. There was differential activation of NF-kB, ERK and Pi3k/Akt pathways between Kras-mutant subtypes. In addition, PD-L1 was upregulated 3-fold by stimulation with IFNγ, independently of the Kras codonsubtypes. Instead, hypoxia significantly increased PD-L1 expression in KrasG12C and KrasG12D cells. Co-culture experiments with human PBMCs from healthy patients were performed to determine the functional effect of altered PD-L1 expression. Increased PD-L1 expression by tumor cells induced by Kras mutations led to decreased PBMCs proliferation and increased apoptosis. An anti-PD-L1 checkpoint inhibitor is currently being tested as single agent or in combination with ERK or PI3K inhibitors in our Kras cell models.
Conclusions: PD-L1 is expressed in 37% of Kras mutant LUAD, suggesting PD-L1 as a therapeutic target in this subset. According to the Kras mutation subtype, potential drugs targeting the NF-kB, ERK or Pi3k/Akt pathways may additionally increase the antitumor adaptive immune responses.
Legal entity responsible for the study: N/A
Funding: Pasteur Hospital, Nice
Disclosure: All authors have declared no conflicts of interest.

breast cancer, locally advanced and metastatic

226PD First line hormone therapy vs chemotherapy for HR+ HER2- metastatic breast cancer in the phase III STIC CTC trial: clinical choice and validity of CTC count

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Background: In patients (pts) diagnosed with HR+ HER2- metastatic BC the choice between by front-line hormone therapy (HT, favored option) or chemotherapy (CT) is based on prognostic factors that are overpassed by CTC count. The STIC CTC trial is a large multicentric phase III randomized trial comparing two strategies to choose the front-line treatment type: decision by clinician vs by CTC levels.
Methods: Clinical/pathological characteristics were registered at time of inclusion, together with the a priori treatment preferred by clinicians (HT or CT). CTC count was then performed by CellSearch® and pts were randomized between a priori treatment and CTC-driven treatment (HT if <5 CTC/7.5ml; CT otherwise). In addition to usual tests, we used multiple correspondence analysis (MCA) to detect and represent underlying structures in our dataset.
Results: This analysis was performed on 530 randomized pts. Main adverse prognostic factors were PS = 2 or 3 (7%), liver (20%) or pleuropulmonary (37%) metastases, >= 3 metastatic sites (34%), lymphocytopenia (39%). HT was the a priori treatment for 371 pts (70%) and CT for 159 pts (30%). Characteristics independently associated with the a priori choice were: age (p = 0.01), center (p < 0.001), prior (neo)adjuvant chemotherapy (HR = 0.47 favoring CT; p = 0.02), elevated SGOT (HR = 0.41; p < 0.001), liver (HR = 0.45; p = 0.005) & bone-only (HR = 3.16 favoring HT; p<0.001) metastases, >10y disease-free interval (HR = 3.45; p = 0.003). 205 patients (39%) had elevated CTC count (≥5 CTC/7.5ml). In MCA, the two first axes were CTC count and prior chemotherapy for early BC, the other clinical and pathological factors being distributed accordingly. Among the 263 pts randomized to the CTC-driven decision arm, a priori HT (186 pts, 71%) was confirmed in 122 pts (68%) and switched to CT in 58 pts (32%); a priori CT (77 pts, 29%) was confirmed in 35 pts only (49%) and switched to HT in 37 pts (51%).
Conclusions: In the absence of any predictive factor, treatment decision is influenced by numerous prognostic factors, among which CTC count appears to play a central role. Patients are followed up to compare the outcome of CTC-driven decision vs a priori clinical decision.
Clinical trial identification: NCT01710605
Legal entity responsible for the study: Institut Curie Funding: INCa
Disclosure: All authors have declared no conflicts of interest.Z

274P Patient preference of trastuzumab administration (SC versusIV) in HER2-positive metastatic breast cancer: Results of therandomised Metaspher study

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Background: HANNAH (NCT00950300) and PREFHER (NCT01401166) international, randomised studies validated the subcutaneous (SC) formulation of trastuzumab as effective and safe as intravenous (IV) and highly preferred by patients in early breast cancer. The present randomized Metaspher trial (NCT 01810393) assessed patient's preference in metastatic setting.
Methods: Patients with HER2-positive metastatic breast cancer who completed a firstline chemotherapy with trastuzumab (IV) and achieved a long term response lasting more than 3 years were randomised to receive 3 cycles of 600 mg fixed-dose adjuvant trastuzumab SC, followed by 3 cycles of standard IV, or the reverse sequence. Primary endpoint was overall preference for SC or IV at cycle 6, assessed by Patient Preference Questionnaire (PPQ). Secondary endpoints included healthcare professional (HCP)satisfaction, assessed by questionnaire; safety and tolerability, assessed by NCI-CTCAEv4.0; quality of life assessed by QLQ C30 questionnaire. The modified-Intent-To-Treat population (m-ITT) included patients who received both routes of administration and who completed the last question of PPQ. The safety population included all enrolled patients who received at least one dose of treatment.
Results: 113 patients were randomised. SC was preferred by 79/92 evaluable m-ITT patients (85.9%, 95% CI [78.8;93.0]; p < 0·001), 13 preferred IV (14.1%, 95% CI[7.0;21.3]). Among patients without preference at baseline (52/89 available data), SC was preferred by 46/52 patients (88,5%, [79.8;97.2]). HCP were most satisfied with SC(56/88 available data, 63.6%, [53.6;73.7]). On the safety population, 108 patients received SC and 111 received IV. Clinician-reported adverse events occurred in 73(67.6%) and 49 (44·1%) patients during the SC and IV periods, respectively; 7 (6.5%)and 4 (3.6%) were grade ≥ 3, 3 (2·8%) and 2 (1·8%) were serious.
Conclusions: Patients preferred trastuzumab SC. The safety profile was consistent with the known IV profile with no safety concerns raised. Next step will assess the follow up of this cohort of long responder patient with metastatic breast cancer. Clinical trial identification: NCT 01810393
Legal entity responsible for the study: Roche
Funding: Roche
Disclosure: X. Pivot: consultant for Roche Amgen Novartis Pierre Fabre Eisai. J-P.Spano: Consultant for Roche.E. Marc, D. Spaeth: Roche. H. Attar-Rabia,C. Benkamoun, L. Dima-Martinez, N. Esposito: Employed by Roche. J. Gligorov:Consultant for Roche, Novartis, Eisai, Pfizer, Genomic Health. All other authors havedeclared no conflicts of interest.

Developmental Therapeutics

375P A phase Ib dose-finding study of alpelisib (ALP; BYL719) andpaclitaxel (PTX) in advanced solid tumors (aST)

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Background: Aberrant activation of the phosphatidylinositol 3-kinase (PI3K)/mammalian target of rapamycin pathway due to alterations in PIK3CA (encodingPI3Kα) frequently occurs in aST.We report safety findings from an ongoing, phase Ibdose-escalation study of ALP (PI3Kα inhibitor) + PTX (NCT02051751).
Methods: Patients (pts) aged ≥18 years with aST (not amenable to resection/progressed on standard therapy), ECOG performance status ≤2, adequate bonemarrow/organ function, and no prior treatment with PI3K or AKT inhibitors wererecruited. The primary objective was to determine the maximum tolerated dose (MTD)and/or recommended Phase II dose of ALP + PTX based on dose-limiting toxicities(DLTs) in Cycle 1. Dose escalation of ALP was guided by an adaptive Bayesian logisticregression model with escalation with overdose control principle.
Results: As of Dec 7, 2015, 19 pts received oral ALP (300 mg [n = 6], 250 mg [n = 4], or150 mg [n = 9] once daily [QD]) and IV PTX (80 mg/m2 once weekly [QW]). Themost common primary sites of cancer were breast (n = 5) and rectum (n = 3).Treatment was discontinued in 18/19 pts due to disease progression (n = 12, 63%), ptdecision (n = 3, 16%), adverse events (AEs; n = 2, 11%; 1 pt for grade [G]3 dehydration,G3 hyperglycemia, and G3 acute kidney injury; 1 pt for G4 neutropenia and G4γ-glutamyltransferase increase), and physician decision (n = 1, 5%). DLTs occurred in5/12 pts in the dose-determining set: 1/1 (100%) pt at 300 mg QD, 2/3 (67%) pts at250 mg QD, and 2/8 (25%) pts at 150 mg QD. Six DLTs were reported: G2hyperglycemia (n = 3), G4 hyperglycemia, G4 leukopenia, and G3 acute kidney injury(each n = 1). The MTD of ALP + PTX (80 mg/m2 QW) was declared as 150 mg QD.All 19 pts had ≥1 treatment-emergent AE. Grade 3/4 AEs occurred in 11 (58%) pts, the most frequent being hyperglycemia (n = 6, 32%), diarrhea, anemia, lymphopenia,
neutropenia, and leukopenia (each n = 2, 11%).
Conclusions: In pts with aST, the MTD of ALP + PTX (80 mg/m2 QW) was 150 mgQD. Due to the challenging safety profile of the combination and lack of available data confirming the pharmacodynamics and/or clinical activity of ALP at 150 mg QD,planned dose expansion in pts with breast cancer and head and neck squamous cellcarcinoma will not go forward.
Clinical trial identification: NCT02051751
Legal entity responsible for the study: Novartis
Funding: Novartis
Disclosure: J. Rodón: Advisory board for Novartis, Lily, Servier, Leti, Oncompass,Orion Pharma. V. Donnet: Novartis Full-time Employee. Y. Han: I am an employee atNovartis and receive a salary from Novartis. L. Blumenstein: I hereby confirm to be aNovartis Pharma AG employee with stock ownership. C. Wilke: Employee of NovartisAG, sponsor of the study. All other authors have declared no conflicts of interest.

397P Phase 1 study of sorafenib and eribulin in patients withadvanced, metastatic or refractory solid tumors

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Background: Combining sorafenib (SOR), an oral multikinase inhibitor approved forhepatocellular carcinoma, renal cell carcinoma, and differentiated thyroid carcinoma, with eribulin mesylate (ERI), a microtubule inhibitor approved for breast cancer (BC), may provide synergistic antitumor activities.
Methods: This phase 1b, open label, dose escalation study evaluated safety,pharmacokinetics (PK), maximum tolerated dose/recommended phase 2 dose (MTD/RP2D), cardiac safety (QT/QTc), and preliminary efficacy of SOR + standard dose ERI(1.4 mg/kg IV on Days [D] 1 and 8 of each 21-day cycle [C]) in patients (pts) with advanced, metastatic, or refractory tumors. Starting SOR dose was 200 mg BID continuously starting on D11 of C1. SOR + ERI-related hematologic and non hematologic dose limiting toxicities (DLT) were assessed in C2. If tolerable, SOR was escalated in new cohorts to 600 mg daily (200 mg AM/400 mg PM) and 400 mgBID. QT/QTc intervals and PK were evaluated respectively in C1 for single dose andC2 for multiple doses. Antitumor activity was assessed by RECIST v1.1. RP2D was confirmed in a MTD expansion cohort (minimum 12 pts).
Results: Of 40 pts treated, 5 received SOR 200 mg BID, 8 received 600 mg/d, and 27received 400 mg BID (MTD), of whom 14 were in the expansion cohort. Of 12 cancer types reported, 62.5% of pts had BC. No DLT was reported in the 200-mg and 600-mgcohorts; 1 DLT (Grade 3 increased ALT) was reported in the 400-mg BID dose escalation cohort and 1 DLT (Grade 3 acute coronary syndrome) in the expansion cohort. Most common drug-related ≥Grade 3 TEAEs were hypophosphatemia (10%)and hypertension (10%) for SOR and neutropenia (25%) for ERI. No significant QT/QTc prolongation was observed; mean QTcF change from baseline was 11.44 ms with ERI alone and 8.25 ms with ERI + SOR. No drug interaction was observed; mean SORAUC was 60.4 mg*h/L for SOR 400 mg BID + ERI and 56.7 mg*h/L for SOR 400 mgBID alone. Respective mean SOR Cmax were 6.8 and 7.7 mg/L. 8 pts had a partial
response (5 confirmed, 3 unconfirmed).
Conclusions: SOR 400 mg BID + standard dose ERI was well tolerated and confirmedRP2D. Toxicities were in line with known SOR and ERI safety profiles. Thus,SOR + ERI would be appropriate to examine in larger studies.
Clinical trial identification: NCT01585870; EudraCT: 2011-005849-12
Legal entity responsible for the study: N/A
Funding: Pharmaceutical Division of Bayer
Disclosure: F.Marmé: Honoraria (presentations and advisory boards): Roche, Novartis,Amgen, AstraZeneca, Eisai, Genomic Health, Celgene. C. Gomez-Roca: Receivedc onsulting fees from Novartis and Sanofi. K. Graudenz, Z. Trnkova: Employee of BayerPharmaAG. F. Huang, J. Lettieri,C. Pena: Employee of BayerHealthCarePharmaceuticals. J. Eucker: Consulting fees: Novartis, Amgen, Roche; Contracted research:Novartis.

endocrine and neuroendocrine tumours

416O Efficacy and safety of pasireotide LAR or everolimus alone, orin combination in patients with advanced carcinoids (NET) ofthe lung/thymus: Results from the randomized, phase 2 LUNA study

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gastrointestinal tumours, colorectal

456O Circulating tumor DNA and circulating tumor cells as predictorof outcome in the PRODIGE14-ACCORD21-METHEP2 phase II trial

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466PD Sorafenib (Soraf) and irinotecan (Iri) combination forpretreated RAS-mutated metastatic colorectal cancer(mCRC) patients: a multicentre randomized phase II trial(NEXIRI 2-PRODIGE 27)

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Background: Sorafenib and irinotecan combination (NEXIRI) showed promising efficacy with a 65% disease control rate (DCR) in pretreated mutated (mt) KRASmCRC. In our previous single-arm phase II study, CCND1 rs9344 A/A polymorphism was found to be a candidate predictive biomarker (Samalin et al. 2014). Our multicentre randomized phase II trial aimed to determine the 2-monthprogression-free survival (2-PFS) of NEXIRI vs Iri or Soraf monotherapies in these patients after failure of all approved active drugs at the time of the study.
Methods: Patients PS ≤ 1 with progressive non-resectable mtKRAS (then RAS) mCRCpretreated with irinotecan, oxaliplatin, fluoropyrimidines and bevacizumab (none with regorafenib), were randomized in 3 arms: NEXIRI (biweekly Iri IV 120, 150, 180mg/m2at C3 combined with a fixed dose of 400mg Soraf twice daily) vs Iri (180mg/m2) alonevs Soraf alone, until progression or toxicity, with cross-over to NEXIRI at progression. Primary endpoint was the 2-PFS (RECIST v1.1). Pharmacokinetic, pharmacogenetics and tissular ancillary studies were performed.
Results:We included 173 patients (age 62 years [31-82]; PS 0/1: 38/61%) betweenJanuary 2012 and July 2014 in 17 French centres. Main results were (median follow-up 17.5 months):
Conclusions: In this randomized study, we confirmed the NEXIRI regimen efficacy for refractory mtRAS mCRC patients and the predictive value of CCND1 rs9344 which may identify patients who benefit from this combination. These results justify comparing NEXIRI to regorafenib monotherapy in CCND1 rs9344 A/A patients. Clinical trial identification: The trial was registered on nicaltrials.gov:NCT01715441
Legal entity responsible for the study: Institut régional du Cancer de Montpellier(ICM)
Fun**d**ing: Grant from the Bayer laboratories
Disclosure: E. Samalin: Honoraria: Lilly, Sanofi, Amgen, Roche Consulting or
Advisory Role: Amgen, Sanofi, Roche Research funding: Bayer (institution) Travel,Accommodations, Expenses: Novartis, Lilly, Ipsen, Roche C. de la Fouchardiere:Consulting or Advisory Role: Amgen, Lilly, Bayer, Roche Research Funding: RocheTravel, Accommodations, Expenses: Roche, Celgene, Amgen. V. Boige: Honoraria:Bayer, Sanofi, Merk-Serono, Daiichi Sankyo Consulting or Advisory Role: Bayer,Amgen Research Funding: Merk-Serono Travel, Accommodations, Expenses:

Merk-Serono, Amgen. H. Senellart: Consulting or Advisory Role: BoehringerIngelheim, Merck, Roche Travel, Accommodations, Expenses: Roche, Pfizer. R.Guimbaud: Consulting or Advisory Role: Ipsen Research Funding: Roche/Genentech(institution) J. Taieb: Honoraria: Merck, Amgen, Lilly, Sanofi, Celgene, Roche Travel,Accommodations, Expenses: Merck, Amgen, Roche. M-P. Galais: Honoraria: Roche. A.Adenis: Consulting or Advisory Role: Bayer, Sanofi Speaker's Bureau: Roche/Genentech Research Funding: Bayer (Institution), Sanofi (Institution). A. Lievre:Honoraria: Merck Serono, Sanofi, Lilly, Amgen, Roche Consulting or Advisory Role:Merck Serono, Sanofi, Lilly, Roche Speaker's Bureau: Celgene Travel,Accommodations, Expenses: Merck Serono, Amgen, Lilly, Roche. F. Di Fiore:Honoraria: Merck, Amgen, Sanofi, Bayer, Novartis, Lilly, Celgene, Roche ResearchFunding: Amgen (Institution), Merck (Institution), Roche (Institution). F. Bibeau:Honoraria: Amgen, Merck, Sanofi, Roche Consulting or Advisory Role: Amgen, SanofiResearch Funding: Roche (Institution) Travel, Accommodations, Expenses: Amgen,Roche T. Mazard: Honoraria: Amgen, Sanofi Research Funding: Roche Parma AG(Institution) Travel, Accommodations, Expenses: Amgen. M. Ychou: Honoraria: Bayer,Merck, Roche Consulting or Advisory Role

490P Phase 2 of intra-arterial hepatic (IAH) bevacizumab withsystemic chemotherapy (CT) in second line treatment of livermetastases of colorectal cancer (LMCRC)

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Background: IAHCT is used in the treatment of LMCRC. Regarding its anti-angiogenic effect bevacizumab (B) is a good candidate for IAH treatment. This phase II evaluate IAH administration of B in second line treatment of LMCRC combined with systemic treatment. We report here the results of the planned interim analysis on toxicity plus those on efficacy as the trial closed prematurely.
Methods: Inclusion criteria: patients (pts) with LMCRC after failure to a 1st line of IVCT; ECOG performance status (PS) 0 or 1; at least one liver lesion evaluable by RECIST; extra-hepatic disease acceptable when limited to one or two lung metastases or lymph nodes potentially accessible to a curative treatment. They had to receive IAH treatment with B, 7.5 mg/kg every 3 weeks, and systemic CT with capecitabine (2 g/m2/day (d) 14 d, followed by 7 d rest) + irinotecan (200 mg/m2 every 21d) or oxaliplati n(130 mg/m2 every 21 d) depending on the 1st line received.
Results: Between 06:2013 and 02/2015, 10 pts from 5 centers were included: 6 men, 4women (median age 61 years); ECOG PS0 (7) and PS1 (3); limited extra-hepatic disease in 4 pts. Median duration of 1st line treatment was 6 months. IAH catheter was implanted surgically in one pt and radiologically in 9. Pts had an average of 6 cycles o fIAH B, 3 received oxaliplatin and 7 irinotecan concomitantly. There was one grade (G)3 allergic reaction to IAH B, one G3 abdominal pain, one G3 mucositis, one G3 nausea and one G3 vomiting events. Related to the use of B, 2 G3 thromboembolic events and3 G3 hypertension were observed. The arterial catheter has to be replaced in one pt and a thrombosis of hepatic artery was observed in a second one preventing continuation of IAH treatment after one cycle. In the 9 evaluable pts, 2 had partial response (22%), 5stable disease (56%) and 2 progressive disease (22%). The median progression-free and overall survival were 5.2 months 95%CI [1.6 – 6.2] and 13.5 months [4.8 – NR].
Conclusions: IAH administration of bevacizumab in pts with LMCRC seems to be feasible with no major side effect. The efficacy reported did not suggest a major effect o fthis treatment that should rather be used in combination with IAHCT with oxaliplatin. We thank the PHRC for its financial support

Clinical trial identification: ClinicalTrials.gov: NCT01677884
Legal entity responsible for the study: Gustave Roussy, Villejuif, France
Funding: Programme Hospitalier de Recherche Clinique

Disclosure: M.P. Ducreux: Receipt of grants/research supports: Roche, Chugai, Pfizer.Receipt of honoraria or consultation fees: Roche, Celgene, Merck Serono. Amgen,Novartis, Sanofi, Pfizer, Lilly, Servier. Spouse: Head of Business Unit, Sandoz. V. Boige:Advisory boards: Bayer, Symposium participation: Bayer, Amgen. D. Malka:Symposium participations: Roche, Amgen, Lilly, Merck Serono, Research funding: Merck Serono, Roche, Amgen Advisory boards: Roche, Amgen. All other authors havedeclared no conflicts of interest.

genitourinary tumours, prostate

722PD PROSELICA: Health-related quality of life (HRQL) andpost-hoc analyses for the phase 3 study assessingcabazitaxel 20 (C20) vs 25 (C25) mg/m2 post-docetaxel (D) inpatients (pts) with metastatic castration-resistant prostatecancer (mCRPC)

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Background: PROSELICA (NCT01308580) was a post-marketing requirement todemonstrate non-inferiority of C20 vs C25 in terms of overall survival (OS) in mCRPCpts who progressed on D.
Methods: Post-D mCRPC pts were randomized 1:1 to receive C25 or C20 (+prednisone). To show non-inferiority of C20 (preservation of ≥ 50% of the incrementalC25 efficacy over mitoxantrone in the TROPIC trial) with 95% confidence interval(CI), hazard ratio (HR) could not

exceed 1.214 under a 1-sided 98.89% CI after interim analyses. Secondary endpoints: progression-free survival (PFS), prostate-specific antigen (PSA) and tumor response (TR), safety, HRQL (Functional Assessment ofCancer Therapy-Prostate [FACT-P] questionnaire) and pain response (PR; Present Pain Intensity score on McGill-Melzack scale). Post-hoc analyses assessed associate on of Grade 3–4 neutropenia on treatment and baseline (BL) neutrophil-lymphocyte ratio(NLR) with OS.
Results: 1200 pts were randomized (598 C20; 602 C25). BL pt characteristics were similarfor C20 and C25. See Table for efficacy results. Rates of Grade 3–4 treatment-emergen adverse events were 39.7% C20, 54.5% C25. Change in FACT-P total score from BL wasnot significantly different for C20 and C25. Grade 3–4 neutropenia on treatment and BLNLR < 3 was associated with increased OS in both arms (Table).
Conclusions: In post-D mCRPC pts, C20 is non-inferior in terms of OS vs C25,meeting the study endpoint. Efficacy parameters favoured C25. Grade 3–4 neutropenia and low NLR may have prognostic value. Funding: Sanofi Genzyme.
Clinical trial identification: NCT01308580
Legal entity responsible for the study: Sanofi Genzyme
Funding: Sanofi GenzymeDisclosure: J.S. de Bono: Received honoraria from and provided a consulting/advisory role for Sanofi Genzyme. D. Ford: Received honoraria from and provided a consulting/advisory role for Janssen and Astellas, and received reimbursement for expenses fromAstellas.J. Carles: Provided a consulting/advisory role for Johson&Johnson, Astellas,Bayer, Amgen, Pfizer, and BMS, and has participated in a speakers bureau for Bayer.G.Kacsó:Was employed by and provided a leadership role for RTC Amethyst, hasreceived honoraria from Sanofi Genzyme, Astra-Zeneca, Janssen, Astellas, has provideda consulting/advisory role for Janssen and Astellas, has received funding from Janssenand CNCSIS.M. Chadjaa: Is an employee of Sanofi Genzyme.W. Zhang: Is an employeeof Sanofi Genzyme and owns stock in Sanofi Genzyme.J. Bernard: Is an employee ofSanofi Genzyme.M. Eisenberger: Provided a consulting/advisory role for and receivedreimbursement for expenses from Astellas, Bayer and Sanofi Genzyme, has receivedhonoraria from Sanofi Genzyme and research funding from Sanofi Genzyme, TokaiPharmaceuticals and Genentech.All other authors have declared no conflicts ofinterest.

723PD Modelling relapse in patients with high-risk localizedprostate cancer treated randomly in the GETUG 12 phase IIItrial reveals two populations of relapsing patients

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Background: The patterns of relapse in patients with high-risk prostate cancer treated with modern therapy are poorly described. In the present study, we aimed to analyse the patterns of relapse in the randomized phase III trial Groupe d'Etude des Tumeur sUro-Genitales 12 (GETUG 12) in patients with high-risk localised prostate cancer
Methods: Patients were enrolled and randomly assigned to receive either androgen deprivation therapy (ADT) with goserelin every 3 months for 3 years combined up front with 4 cycles of docetaxel and estramustine (ADT + DE) or ADT alone, pluslocal therapy. We analysed the pattern of second event-free-survival (PFS2) in patientswith biochemical progression (bPFS). Adjusting factors were stratification factors (Tstage, Gleason score, baseline PSA, and pN status) and treatment.
Results: 413 patients were randomized from 2002 to 2006, 206 treated with ADT alone and 207 with ADT + DE. Median follow-up was 8.8 years (IQR: 8.1-9.7). A total of 130patients exhibited biochemical relapse, with a median bPFS of 5 years (range: 0.23-10.4)for relapsing patients. 77/130 patients subsequently developed a second event: metastatic progression (53), clinical progression (13) and death (7). The analysis of relapsing patients revealed the following data: 1) the median time from biochemical failure to a clinical event was 2 years [95%CI: 1.07 – 2.91]; 2) biochemical relapses were rare (n = 27; 21%) within the first 3 years (<3 yrs) with most relapses (n = 103; 79%) occurring after 3 years (≥3yrs); 3) the timing of relapse (<3 yrs) exerted a major prognostic impact: 26/27 patients(96%) relapsing within 3 yrs and 51/103 patients (50%) relapsing ≥3 yrs developed a second event (adjusted hazard ratio: 0.53 [95% CI: 0.32-0.88], p = 0.014).
Conclusions: This analysis of the GETUG 12 trial demonstrates that overall, a clinical event is to be expected, with a median time of 2 years in patients with high-risk localised prostate cancer who develop a biochemical relapse, and that the timing of this relapse is highly prognostic with twice as many clinical events likely to occur inpatients relapsing within the first 3 years.
Clinical trial identification: GETUG 12: ClinicalTrials.gov NCT00055731
Legal entity responsible for the study: Institut Gustave Roussy
Funding: N/A
Disclosure: A. Flechon: Sanofi. S. Oudard: Sanofi, Bayer, Astellas, Janssen. K. Fizazi:Participation to advisory boards and honorarium: Sanofi. All other authors havedeclared no conflicts of interest.

725PD Pembrolizumab for patients with advanced prostateadenocarcinoma: Preliminary results from the KEYNOTE-028study

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Background: Therapies currently available for castrate-refractory prostate cancer(CRPC) provide only modest clinical benefit. Expression of the programmed death 1(PD-1) receptor and its ligand, PD-L1, has been reported in CRPC. Pembrolizumab, ananti–PD-1 antibody, blocks the interaction between PD-1 and PD-L1. KEYNOTE-028(NCT02054806) is a nonrandomized, phase 1b trial to evaluate the safety and efficacy yof pembrolizumab in 20 advanced solid tumor cohorts. Herein are the results from the prostate adenocarcinoma cohort of this study.
Methods: Key eligibility criteria included advanced adenocarcinoma of the prostate, failure of standard therapy, measurable disease per RECIST v1.1, ECOG PS 0-1, andPD-L1 expression in ≥1% of tumor or stroma cells by immunohistochemistry. Pembrolizumab 10 mg/kg was administered every 2 weeks (wk) for up to 24 months(mo) or until disease progression (PD), intolerable toxicity, death, or withdrawal of consent. Stable patients (pts) with PD could remain on treatment until PD was confirmed by a follow-up scan. 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 review. As an exploratory objective, a NanoString platform was used to assess baseline tumor tissue for the gene expression profile (GEP) of an 18-gene panel hypothesized to be associated with a Th1-derived IFN-γ immune response.
Results: Of the 23 pts enrolled in this cohort, median age was 65 years, 74% had an ECOG PS of 1 (1 pt had an ECOG PS of 2), and 74% received ≥2 prior therapies for metastatic disease. As of February 17, 2016, median follow-up duration was 33 wk(range, 6-79 wk). Fourteen pts (61%) had treatment-related adverse events (TRAEs),most commonly nausea (n = 3, 13%). Three pts (13%) had grade 3-4 TRAEs; 1 pt had grade 3 fatigue, 1 pt had grade 3 peripheral neuropathy, and 1 pt had grade 3 asthenia and grade 4 lipase increase. No pts died or discontinued pembrolizumab because of aTRAE. Three pts had a confirmed PR, for an ORR of 13% (95% CI, 3%-34%); median duration of response was 59 wk (range, 28-62 wk). Stable disease rate was 39% (n = 9;95% CI, 20%-61%). Median OS was 8 mo, and the 6-mo PFS rate was 39%. Two pts remained on treatment at data cutoff. Exploratory assessment of the relationship between GEP score and clinical outcome revealed the putative T cell inflamed signature to be associated with better clinical outcome, consistent with pembrolizumab findings published previously.
Conclusions: Pembrolizumab produced durable responses among heavily pretreated pts with advanced PD-L1–positive prostate cancer. Treatment was associated with afavorable side-effect profile.
Clinical trial identification: NCT02054806
Legal entity responsible for the study: Merck & Co. Inc.
Funding: Merck & Co., Inc.
Disclosure: C. Massard: Advisory Board Member: Astra Zeneca, Bayer, Celgene,Genentech, Ipsen, Jansen, Lilly, Novartis, Pfizer, Roche, Sanofi, Orion, MedImmune,New Oncology, DebioPharm.M. Gould, P. Qiu, S. Saraf, S. Keefe: Employee, stockownership Merck & Co., Inc.S.A. Piha-Paul: Corporate-sponsored research:GlaxoSmithKline, Novartis, Puma Biotechnology, Inc., Merck, Sharp and Dohme,BioMarin Pharmaceutical, Inc., Principia Biopharma, Inc., Abbvie, XuanZhuBiopharma, Helix BioPharma Corp., Incyte, Inc., Curis.All other authors have declaredno conflicts of interest.

761P How should we treat castration-resistant prostate cancerpatients who have received androgen deprivation therapy(ADT) plus docetaxel upfront for hormone-sensitive diseae?Mature analysis of the GETUG-AFU 15 phase III trial

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Background: Since 2015, docetaxel chemotherapy, combined with ADT, is consideredthe standard of care in fit men with metastatic hormone-naive prostate cancer (mHNPC), based on data from three phase III trials (GETUG-AFU 15, CHAARTED, and STAMPEDE). No data are currently available regarding activity of 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, physician assessment ofclinical benefit, and time to events), and toxicity (NCI-CTC grading).
Results: 245 pts received at least one anticancer treatment at CRPC progression. The treatments most frequently used and their efficacy are detailed in the Table. Toxicity was mild, with only rare grade 3-4 events (17%). Median overall survival measured after the onset of CRPC was respectively 2.29 years (IC95% [1.84-2.59]) and 1.97 years (IC95% [1.64-2.73]) in the ADT and ADT + D arms.
Conclusions: In this retrospective analysis, anticancer activity was suggested with androgen receptor axis-targeted agents even in patients with metastatic prostate cancer treated upfront with ADT + docetaxel. We observed that docetaxel rechallenge had rather limited activity in this setting.
Clinical trial identification: NCT00104715; release date: 2013 Februray (LancetOncol)
Legal entity responsible for the study: Unicancer
Funding: French Health Ministry and Institut National du Cancer (PHRC),Sanofi-Aventis, AstraZeneca, and Amgen
Disclosure: F. Joly: Roche, Pfizer, Novartis, Sanofi, Jansen, Astellas.M. Soulié: Amgen,Astellas, Astra Zeneca, Ferring, Glaxo Smith K, Ipsen, Jansen, Keocyt, Novartis, PierreFabre, Sanofi, Takeda, Zambon.B. Laguerre: Pfizer, Novartis, Jansen.K. Fizazi:Participation to advisory boards and honorarium : Sanofi, Janssen, Astellas.All otherauthors have declared no conflicts of interest.

genitourinary tumours, prostate

829P Denosumab in patients with bone metastases from renal-cellcarcinoma treated with anti-angiogenic therapy:a retrospective study from the GETUG (Groupe Etude desTumeurs Uro Genitales)

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Background: Metastatic renal-cell carcinoma (mRCC) treatment relies onanti-angiogenic therapies. Bone metastases occur in nearly 30% of mRCC and caninduce symptomatic skeletal-events (SSE) such as pain requiring radiotherapy, pathologic fractures, and spinal cord compression. SSE can be prevented using bone-targeted agents, e.g. bisphosphonates or denosumab. Data about denosumab and anti-angiogenic combination are scarce.

Methods: This multicenter retrospective study led by GETUG included mRCC patients (pts) who received anti-angiogenic therapies associated with denosumab from January 2013 to December 2015. The primary endpoint was toxicity related todenosumab, especially osteonecrosis of the jaw (ONJ) and hypocalcaemia.

Results: 37 pts were identified and 36 analyzed. The mean age was 60.9 year-old (range42-81). Twenty-four pts (68%) had an odontological consultation before denosumab introduction and 20 pts (58.3%) had a dental panoramic radiography. Five pts (13.9%) developed an ONJ, among them 3 had a dental extraction while on denosumab treatment. Only one out of the 5 pts has completely recovered from his ONJ. No grade3-4 hypocalcaemia was reported. SSE occurred in 22 pts (61.1%) including bone pain requiring radiation, clinical fractures, and spinal compression in 22, 3, and 2 pts, respectively.

Conclusions: In this real life population, the incidence of SSE was very high in mRCCpts with bone metastases. The combination of denosumab with anti-angiogenic drugs was associated with a high incidence of ONJ that may have been favored by denta lextraction while on treatment. The present study underlines the need to improvestrategies to prevent the onset of SSE in this population of pts.

Legal entity responsible for the study: N/A

Funding: GETUG

Disclosure: A. Guillot: board PFIZER. S. Negrier: honoraria from Pfizer, Novartis etBMS. D. Pouessel: Board: roche, astellas, Lilly, Novartis, Sanofi Advisory: MSD,AstraZeneca. Speaker : Astellas, Janssen, Boehringer-ingelheim, Sanofi. C. Chevreau:board advisory: Pharmamar Inc, Novartis Inc. L. Albiges: consultaant or advisory role:novartis, pfizer, amgen, BMS, Bayer, Sanofi, Cerulean. K. Fizazi: consultant/advisor forAmgen Inc.,Novartis,Clovis, Pfizer, CSL, Behring, and Bayer- GlaxoSmithKline, andGenentech- speakers' bureau for Genomic Health research funding from Amgen Inc.,Novartis, Bayer, and Puma. All other authors have declared no conflicts of interest.

gynaecological cancers

859PD The CHIVA study: a GINECO randomized double blind phase IItrial of nintedanib versus placebo with the neo-adjuvant chemotherapy (NACT) strategy for patients (pts) with advanced unresectable ovarian cancer (OC). Report of theinterval debulking surgery (IDS) safety outcome

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Background: Improving NACT response rate in pts with OC could lead to increased complete resection rate (CC0) at IDS and better survival. Bevacizumab has been shown to increase response rate to chemotherapy both in first-line (ICON7) and in relapse(OCEANS and AURELIA). Due to concerns about bevacizumab impact on IDS woundhealing, the safety and efficacy of nintedanib, an orally available anti-VEGF/PDGFR/FGFR tyrosine kinase inhibitor with a short half-life was explored in the neo-adjuvantsetting.

Methods: All patients underwent laparoscopy and their disease was considered as unresectable (impossibility to achieve CC0 at primary surgery). Eligible patients were randomized (2:1) to receive 3 cycles of NACT before IDS and 3 cycles of chemotherapy after IDS with carboplatin + paclitaxel and nintedanib or placebo (at cycle 1&2, 5&6and at maintenance therapy as single agent during 2 years). The aim of IDS was to achieve CC0. Surgical complications were scored according to Clavien Dindo classification.

Results: A total of 188 patients were included and 121 (64%) patients underwent IDS(49 in placebo arm and 72 in experimental arm). Pts characteristics are well balanced between both arms. No significant difference was observed between the placebo and the nintedanib arm in terms of operating procedure duration (360 vs 330 minutes) andper-operative (18 vs 13%) complications. Bleeding (2 vs 9% of the pts), blood losses (500 vs 675 ml), and transfusion rate (12 vs 26% of the pts) were slightly less frequent in the placebo arm. Around half of the patients experienced at least one postoperative complication: 53% versus 47% in the placebo and nintedanib arm respectively. They were mostly of grade I-II (86% grade I-II, 14% grade III-IVa) with no significant difference between the two arms in type and grade of postoperative complications.

Conclusions: Compare to placebo, the addition of the anti-VEGF nintedanib toneo-adjuvant chemotherapy did not significantly increase the rate of per-operative andpost-operative complications of the interval debulking surgery.
Clinical trial identification: NCT01583322
Legal entity responsible for the study: ARCAGY-GINECO
Funding: Boehringer Ingelheim
Disclosure: All authors have declared no conflicts of interest.

melanoma and other skin tumours

1138P Cobimetinib plus vemurafenib to treat unresectable ormetastatic melanoma: Data from the French temporaryauthorization for use

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Background: Given the positive findings from the coBRIM phase III study havingassessed cobimetinib (C) plus vemurafenib (V) in patients (pts) with BRAF V600mutation-positive unresectable locally advanced or metastatic melanoma, a Temporary Authorization for Use (TAU) program (pre-approval access to new treatment options where unmet medical need exists) has been settled in France for cobimetinib from 27Apr 2015 to 04 Jan 2016.
Methods: Analysis was performed in pts with approved treatment-access delivered within TAU. Specific forms had to be completed at C initiation (in combination withV) and monthly after first treatment intake. All adverse events (AEs) had to be reported during pts' follow-up.
Results: A total of 376 pts had approved early access to the combined therapy (C plusV). Following baseline data were available for 328 pts (87%). Mean age was 57 ± 15years and 59% were male. A total of 290 pts (89%) had stage IV melanoma (M1a: 11%,M1b: 13%, M1c: 64%) and 79 pts (24%) presented with brain metastasis. During follow-up, 280 AEs were reported in 134 of 376 pts (36%), including 208 (74%)C-related AEs reported in 108 pts (29%) and/or 160 (57%) V-related AEs reported in82 pts (22%). Among the 101 (36%) serious AEs (SAEs) reported in 63 pts (17%), 67SAEs (24%) reported in 42 pts (11%) were assessed as related to C. Twenty-two AEs(8%) reported in 12 pts (3%) led to permanent C discontinuation. Fifty-three predefined specific AEs (19%) were reported in 49 pts (13%): 23 increased creatine phosphokinase (including 2 SAEs), 12 photosensitivity reactions (7 SAEs), 7 retinal detachments (3 SAEs), 7 renal failures (3 SAEs), and 4 left ventricular ejection fraction decreases (1 SAE). No squamous cell carcinoma nor C-related death were reported during follow-up.
Conclusions: These real-life data from this French TAU program are consistent withsafety data collected during clinical development program and showed no new safety signal for C when combined with V to treat pts with unresectable or metastatic melanoma.
Legal entity responsible for the study: Roche S.A.S
Funding: Roche S.A.S
Disclosure: N. Meyer: Financial interest for professor Nicolas Meyer, in Melanoma,with differents pharmaceuticals companies: -Roche -Novartis -BMS -MSD –Amgen-GSK. D-M. Anne-Bénédicte: Financial interest for doctor Duval Modeste withdifferents pharmaceuticals laboratories: -Roche -Novartis -BMS -Abbvie -Janssen Cilag-Pfizer. B. Dreno: Finantial interest for professor Dreno Brigitte with differentspharmaceuticals companies: -Roche -Novartis -BMS -Amgen. C. Lebbe: Financialinterest in Melanoma for Doctor Celeste Lebbe: -Roche -Novartis -BMS –MSD-Amgen. O. Zehou: Financial interest for doctor Ouidad Zehou in melanoma, withother pharmaceuticals laboratories: Roche Novartis BMS. A. Gorana: Financial interestfor Adrian Gorana: He is doctor in drug monitoring for Roche S.A.S. M. Mouri:Financial interest for Mehdi Mouri: He works for Roche S.A.S, he is doctor andmedical responsible in dermatology and hematology. A. Bardet: Financial interest inMelanoma for Aurélie Bardet: She is Bio-statistician for Roche S.A.S. M. Moreau:Project manager for Roche S.A.S. C. Mateus: Financial interest for doctor ChristinaMateus in melanoma with other Pharmaceuticals companies: -Roche

1143P Lower risk of cutaneous squamous cell carcinomas inducedby vemurafenib in non melanoma patients

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Background: Cutaneous squamous cell carcinomas (cSCCs) occur in about 20% ofmelanoma (M) patients (pts) treated with vemurafenib (V), mostly within the first 3months.We aimed to determine the frequency of cSCCs in non-M pts treated by V in the AcSé-V French national phase II trial and to study their clinical, pathological and molecular characteristics.
Methods: Pts included in the AcSé-V trial had a dermatological monitoring under the supervision of the French "Groupe de Cancérologie Cutanée". Only pts with a follow-up of ≥4 months and without a history of M are included. Pathological reports of resected cSCCs and precursors were analysed by a pathologist. Central pathological review and molecular characterization of cSCCs will be performed. Frequency of cSCCswas compared to BRIM 3 published data.
Results: Among 56 pts included in the AcSé trial, six pts (11%; 4F,2M) treated for aBRAF V600E-mutated lung, thyroid or brain tumour developed 10 cutaneous neoplasms. Median size was 5.5 mm (range, 5-10 mm). Location was upper (n = 4) or lower (n = 3) extremities, head and neck (n = 2), and trunk (n = 1). There were 8cSCCs, 1 papilloma with a keratoacanthoma-like architecture and 1

preepitheliomatous keratosis. Five pts (9%) of median age 76 years old (range, 23-83 years) had cSCCs (multiple cSCCs in 2 pts). Pathological review of cSCCs (7/8 available) showed crateriform (n = 4) or papilliform (n = 2), poorly (n = 1) or well-differentiated (n = 6)cSCCs. The median time to first diagnosis of cSCC or precursor lesion was 71 days(range, 29-161 days); 5/6 pts had a phototype 3; none had a medical history of skin cancer but 3 presented actinic keratosis before V initiation.
Conclusions: V-induced cSCCs seem to have similar pathological characteristics in M and non-M pts. The lower frequency of cSCCs in non-M pts compared with M pts in BRIM 3 (p = 0.039) might be due to differences in risk factor frequencies. Potential risk factors of V-induced cSCCs are older age and preexisting actinic keratosis. Analysis offinal data might help for dermatological monitoring.
Clinical trial identification: NCT02304809
Legal entity responsible for the study: UNICANCER, GCC
Funding: UNICANCER
Disclosure: X. Troussard: Advisory Board : Gilead. Roche. Janssen. S. Leboulleux:Consulting : Genzyme, Sanofi, Astra Zeneca. Travel : Genzyme, Sanofi,Bayer. D. Malka: Honoraria : Roche, Amgen, Bayer, Teva, Celgene, Lilly, Merck, MerckSerono, Sanofi-Aventis. Consulting : Roche, Merck. Travel : Roche,Sanofi-Aventis. S. Dalle: Received research grant from Roche-Genentech. J-Y. Blay:Advisory Board: Roche, Novartis, Bayer, MSD, Lilly, Pharmamar, Deciphera.Corporate-sponsored Research: Roche, Novartis, Bayer, MSD, Lilly, Pharmamar. Allother authors have declared no conflicts of interest.

NSCLC, metastatic

LBA47_PR - Selumetinib in combination with docetaxel as second-line treatment for patients with KRAS-mutant advanced NSCLC: Results from the phase III SELECT-1 trial

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Boston, US, Amsterdam, NL, Marseille, FR, Málaga, ES, Toulouse, FR, Perugia, IT, Saint Petersburg, RU, Manchester,GB, Köln, DE, Madrid, ES, St. Petersburg, RU, Royston, GB, Melbourne, VIC/AU,Macclesfield, GB, Cambridge, GB, Gaithersburg, MD/US, Leuven, BE

1202O Clinical and biological characteristics of non-small cell lung cancer (NSCLC) harbouring EGFR mutation: Results of the nationwide programme of the French Cooperative Thoracic Intergroup (IFCT)

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1234P Osimertinib in EGFR T790M positive advanced NSCLC(aNSCLC) – real–life data from the French temporaryauthorization for use (ATU) program

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Background: Osimertinib, an oral, irreversible EGFR-TKI selective for sensitizing(EGFRm) and T790M resistance mutations, has been shown to be effective and welltolerated in clinical studies for pts with EGFR T790M positive aNSCLC. Pts in France had early access to osimertinib through an ATU program before approval.
Methods: Pts with EGFR T790M positive aNSCLC were eligible if they had receivedprior EGFR-TKI therapy and a platinum-based chemotherapy (CT) or had CT intolerance; additional lines of therapy were permitted. T790M testing was performed by INCA (French National Cancer Institute) certified platforms.
Results: From 07/04/2015 to 24/03/2016, 134 centres enrolled 364 pts; 99% had stag eIV adenocarcinoma and 38.5% had brain metastases. Median therapies prior too simertinib was 2 (1–9). The most frequent prior therapies were 1st line EGFR-TKI(66.2%; median duration 15.2 mo) and 2nd line platinum-based CT (42.0%).
As of March 2016, 350 pts were treated, 14 excluded (prescriber decision / pt death).61% were treated ≥3 mo, 30% ≥6 mo and 14% ≥9 mo. Overall response rate (ORR) in123 pts evaluable was 61.8% (95% CI 53, 70) (CR 5.7%, PR 56.1%). Disease control rate(CR + PR + SD) was 80.5% (99/123). 309/350 pts (88.3%) ongoing at data cutoff, 23 pts withdrawn for disease progression. Investigator reported safety data (n = 350) showed36 pts (10.3%) experienced ≥1 treatment-related AE, 13 pts (3.7%) had AEs leading to discontinuation. 12 pts (3.4%) died (1 death drug related, attributed by investigator). 9pts (2.6%) had AEs resulting in dose reductions; 3 pts (0.9%) had temporaryinterruptions.

Conclusions: In pts with EGFR T790M positive a NSCLC, osimertinib had antitumouractivity with a similar ORR to that in clinical studies, with good tolerability .Identification of eligible pts is feasible in daily practice at tumour progression byT790M testing on rebiopsy or using ctDNA.
Clinical trial identification: NL 46006-46007 September 2015
Legal entity responsible for the study: AstraZeneca
Funding: AstraZeneca
Disclosure: D. Planchard: Personal fees from AstraZenaca, Boehringer, Clovis,Novartis, Sanofi aventis, BMS, Roche, Lilly, Pfizer, and grants from Novartis. M. Pérol:Personal fees from Astra-Zeneca, Clovis Oncology, Roche, Boehringer-Ingelhaim,outside the submitted work. A. Cortot: Personal fees from Astrazeneca. J. Cadranel:Personal fees from BI, Roche, AstraZeneca. R. Schott: Personal fees from Roche SASand Pierre Fabre; and non-financial support from Roche SAS, Pierre Fabre, Novartis,Astra Zeneca, Lilly, and Amgen. E. Dansin: Personal fees from AstraZeneca, Roche andClovis. D. Moro-Sibilot: Personal fees from Astrazeneca, Pfizer, Novartis, Clover, ElLilly, Roche, and Ariad. J-C. Soria: Personal fees from AstraZeneca, Pfizer, Pierre fabre, Roche, Sanofi, and Servier. M. Coudurier: Personal fees and non-financial supportfrom Aztra Zeneca, Roche, BI, Clovis, during the study; grants, personal fees and non-financial support from Msd, BMS, Roche, Lilly, BI, Amgen, outside the submittedwork. A. Gourion: Personal fees from AstraZeneca, during the conduct of thestudy. N. Varoqueaux: Other from AstraZeneca, during the conduct of thestudy. C. Chouaid: Grants, personal fees and nonfinancial support from Aztra Zeneca,Roche, BI, Clovis, during the conduct of the study; grants, personal fees and nonfinancial support from MSD, BMS, Roche, Lilly, BI, Amgen, outside the study. Allother authors have declared no conflicts of interest.

1245P Phase I, safety, tolerability and preliminary efficacy study oftremelimumab (Trem) in combination with gefitinib (Gef) inEGFR-mutant (EGFR-mut) NSCLC (GEFTREM)

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Background: A Phase I open-label multicenter study was initiated to evaluate theassociation of T-cell lymphocyte-4 (CTLA-4) inhibitor Trem with Gef in progressingEGFR-mut NSCLC (NCT02040064).
Methods: Key inclusion criteria included advanced NSCLC with an EGFR-mut, progression after a response on any prior EGFR TKI (first line or beyond), adequate PS(0-1). The primary objective was to determine the safety and tolerability of the combination of Gef (oral 250mg once-daily) with escalating doses of Trem (starting dose of 3mg/kg IV every 4 weeks for 6 cycles and beyond every 12 weeks) and toestablish a recommended phase 2 dose (RP2D). A rolling 6 design and a dose limiting toxicity (DLT) period of 42 days were applied. Three escalating doses of Trem we repre-planned (3, 6 and 10mg/kg).
Results: Between January, 2014 and March, 2015, 26 stage IV pts (20pts in the escalating dose cohorts and 6 in expansion cohort pts at RP2D) received at least one dose of Trem (median age of 66 years, female 65%, never smoker 61% and 61% had received ≥2 lines). Previous line was an EGFR-TKI in 77% of pts. DLTs occurred in 5pts, 1 at 3mg/Kg (grade 3 colitis), 2 at 6mg/Kg (one grade 3 colitis and one AST-ALT increase grade 3 in expansion cohort) and 2 at 10mg/Kg (one grade 3 diarrhea and one AST-ALT increase grade 3) of Trem. All toxicities were reversible with discontinuation of Trem. Most common (≥20%) adverse events (AEs/grade 3-4 AEs) were diarrhea(92%/27%), asthenia (77%/4%), dry skin (54%/4%), nausea (38%/4%), anorexia (27%/8%), dyspnea (42%/0%), colitis (19%/4%), and vomiting (27%/4%). No pneumonitis or increases in cutaneous toxicity related to treatments were observed. Twenty four pts were evaluable for response. The best overall response was stable disease in 67% of pts(18/24pts, 69% at 3mg/Kg, 50% at 6mg/Kg and 80% at 10mg/Kg). All pts discontinued treatment after median duration of 8 weeks (range: 2 to 77 weeks), most frequently dueto disease progression (60% of pts).
Conclusions: The recommended dose of Trem in phased combination with Gef inEGFR-mut pts with NSCLC was identified as 3mg/kg. Antitumor activity was stabledisease in two thirds of pts. The safety profile was consistent with the previouslydefined AE profile.
Clinical trial identification: NCT02040064
Legal entity responsible for the study: Gustave Roussy
Funding: Gustave Roussy was the sponsor and coordinator of this trial. This researchwas conducted with support from AstraZeneca.
Disclosure: D. Planchard: Advisory Board : Astrazeneca, Boehringer, Pfizer, Roche,BMS, Merck, Novartis, Sanofi-aventis, Lilly, Clovis. F. Barlesi:Astrazeneca. C. Gomez-Roca: advisory board Sanofi and Novartis. J. Mazieres,L. Greillier: advisory board Atrazeneca. A. Varga, J-C. Soria: advisory board Atrazenecaand Clovis. B. Besse: Resear

1285TiP IFCT-1003 LADIE trial: Randomized phase II trial evaluatingtreatment with EGFR-TKI versus EGFR-TKI associated withanti-estrogen in women with non-squamous advancedstage NSCLC

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Background: The incidence of lung cancer is increasing dramatically in women and displays some specific epidemiological, radiological, clinical and pathological characteristics. Two main mechanisms emerged from recent findings in the field of lung carcinogenesis in women: the preferential involvement of the EGFR pathway and the potential impact of hormonal factors. The interaction of estrogen receptors with growth factor receptor signalling has also been shown. Preclinical data have shown that the combination of an EGFR-Tyrosine Kinase Inhibitor (TKI) with an anti-estrogen could overcome resistance to EGFR-TKI by postponing the reactivation of thePI3K-AKT pathway

through the estrogen-mediated non-genomic pathway.Trial design: We launched an open-label phase II randomized trial dedicated to women with advanced stage adenocarcinoma. Patients are treated by gefitinib (250 mg/d) vs. gefitinib + fulvestrant 500 mg MI / month (with a supplementary dose at day 15)in the EGFR mutated group (EGFR +) in first or second line setting and by erlotinib(150 mg/d, according to marketing authorization at trial initiation) vs. erlotinib + fulvestrant in the EGFR wild-type group (EGFR WT) in second or third line setting. Treatments are given until progression or unacceptable toxicity. Follow-up isperformed in both arms every month to minimize the potential bias due to monthly fulvestrant injection. Primary objective is progression-free survival (PFS) at 3 and 9months for EGFR WT and EGFR + patients, respectively. Secondary objectives aresafety, overall survival and quality of life. Exploratory objective is biomarkers analysis. The main inclusion criteria are histologically-confirmed non-squamous NSCLC, available tumor tissue for EGFR mutation analysis, post-menopausal women, PS 0-2.The study has been approved by all ethical committees. An ancillary study is ongoing in the EGFR mutated cohort to detect and monitor the EGFR T790M mutation in these rum. First patients have been enrolled in May 2012. To date, 326 patients (162EGFR + , 164 EGFR WT) have been enrolled and 394 (204 EGFR +, 190 EGFR WT)are expected.
Clinical trial identification: NCT01556191
Legal entity responsible for the study: N/A
Funding: AstraZeneca, Ligue Nationale Contre le Cancer
Disclosure: All authors have declared no conflicts of interest

1290TiP ALUR: a phase 3 study of alectinib versus chemotherapy inpreviously treated ALK+ non-small cell lung cancer (NSCLC)

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Background: Crizotinib is the current standard of care for NSCLC patients (pts) withALK+ disease. However, most pts who get crizotinib will progress within a year.Further, until recently, crizotinib was only approved in Europe as 2nd-line treatment
after failure of 1st-line platinum-based doublet chemotherapy (PDC), so many pts whore lapse after crizotinib have also been pre-treated with PDC. Most will go on to receive standard relapse chemotherapy (SRC), e.g. pemetrexed or docetaxel. The ALKinhibitor alectinib was recently approved by the FDA based on the efficacy/safety shown in two phase 2 single-arm studies of pts with pre-treated ALK+ NSCLC(NP28673: Ou et al, JCO 2015; NP28761: Shaw et al, Lancet Oncol 2016). However, itis not yet confirmed whether this approach would be more or less effective than SRC inthe 3rd line for ALK+ NSCLC pts who relapse after both PDC and crizotinib. Trial design: ALUR (NCT02604342) is a phase 3 open-label randomised study in ptswith advanced or metastatic ALK+ NSCLC and ECOG PS 0–2 who have had one prior line each of PDC and crizotinib. Pts (n = 120) are randomised 2:1 to receive alectinib600mg BID or SRC (pemetrexed 500mg/m2 q3w or docetaxel, 75mg/m2 q3w; at investigator's discretion) until progression, death or withdrawal. Crossover from SRCto alectinib is permitted on RECIST progression. At the investigators' discretion, alectinib can be continued beyond progression for patients with clinical benefit. FPIwas in Oct 2015 and LPI is expected in Q3 2016. The primary endpoint is progression-free survival (PFS) by investigator in the ITT population. Secondary endpoints include objective response rate (ORR) in the central nervous system (CNS) for pts with measurable CNS metastases (mets) at baseline; PFS by independent review committee (IRC); ORR, disease control rate (DCR) and duration of response (DOR) by investigator and IRC; time to CNS progression, CNS DOR and DCR by investigator and IRC; overall survival; health-related quality of life; time to symptom deterioration ;and safety. Pts will be stratified by ECOG PS (0/1 vs 2), presence of baseline CNS mets and history of CNS radiation, with caps to ensure ≥50% have baseline CNS mets and both types of SRC are equally represented.
Clinical trial identification: NCT01801111 [NP28673] and NCT01871805[NP28761].
Legal entity responsible for the study: F. Hoffmann-La Roche Ltd
Funding: F. Hoffmann-La Roche Ltd
Disclosure: J.Wolf: Advisory Boards for AstraZeneca, Boehringer Ingelheim, Novartis,Pfizer and Roche. C. Revil: Roche Employee and Stock Ownership. A. Kotb: Employeeof Roche. A. Zeaiter: Roche Employee, Stock Ownership and Roche Leadership. Allother authors have declared no conflicts of interest.

sarcoma

1396O Results of a prospective randomized phase III T-SAR trialcomparing trabectedin vs best supportive care (BSC) inpatients with pretreated advanced soft tissue sarcoma(ASTS)

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1397O The nationwide cohort of 26,883 patients with sarcomastreated in NETSARC reference network between 2010 and2015 in France: major impact of multidisciplinary boardpresentation prior to 1st treatment

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1406P Update of the T-DIS randomized phase II trial: Trabectedinrechallenge versus continuation in patients (pts) withadvanced soft tissue sarcoma (ASTS)

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Background: Trabectedin (T) maintenance beyond 6 cycles (cy) of treatment in responding pts with ASTS is associated with improved progression-free survival (PFS)vs T discontinuation (Le Cesne, Lancet Oncol 2015). The impact of T rechallenge after progressive disease (PD) was prospectively analyzed by the French Sarcoma Group inthe national randomized phase II trial (T-DIS; NCT01303094).
Methods: After the initial 6 cy of T (1.5 mg/m2 as 24-h infusion every 3 weeks) pts free of PD were randomly assigned either to continuous treatment with T (C arm; immediate 7th cy) or therapy interruption (I arm). Pts allocated to the I arm could restart T in case of PD (7th cy at the time of PD). Here we report updated outcomes inboth arms obtained either from randomization or from the 7th cy date.
Results: From 2/2011 to 3/2013, 178 pretreated pts have been enrolled. Median age and performance status were 57 years (range 19-82) and 1 (range 0-3), respectively. Most pts had leiomyosarcoma (30.0%), liposarcoma (18.0%) or synovial sarcoma (12.0%).53/178 (29.7%) non progressive patients were eligible for randomization after 6 cy of T,27 and 26 non progressive pts were randomized to C and I arms, respectively. T has been restarted in 22/26 progressive pts in I arm whereas 25 out of 27 pts of the C arm immediately continued T. Median number of cy after randomization was similar I nboth arms (5 vs 6 cy, p = 0.96). From the date of randomization the median PFS was5.3 vs 3.5 months (p = 0.019) in the C and I arm, respectively, and 6-month PFS was48.2 vs 19.2%. From the date of the 7th cy comparable median PFS (4.2 vs 4.8 months, p = 0.88) and 6-m rates of PFS (45.8% vs 34.7%) were observed in C and I arm, respectively. From the 7th cycle, a favorable trend in longer median OS was observed inC arm (26.0 vs 14.9 months), which did not reach the level of significance (log-rank test p = 0.14) due to the small sample size. Grade ≥3 toxicity rates were not significantly different between the two arms (36.0% vs 38.1%) after T rechallenge (p = 0.88).
Conclusions: Though T remains an active agent at rechallenge, we do not recommend trabectedin discontinuation in pts experiencing stable disease or partial response since interruption of T resulted in a rapid PD in most pts.
Clinical trial identification: EudraCT NCT01303094
Legal entity responsible for the study: Centre Oscar Lambret
Funding: Centre Oscar Lambret
Disclosure: All authors have declared no conflicts of interest.

thoracic malignancies, other

1509PD Quality of resection and outcome in stage III thymicepithelial tumors (TET): A retrospective analysis of 150cases from the national network RYTHMIC experience

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Background: Stage III TET represents a heterogeneous population and their optimal approach remains unclear; most of the available literature is composed of small series spanned over extended periods of time. RYTHMIC (Réseau tumeurs THYMiques et Cancer) is a French nationwide network for TET with the objective of territorial coverage by regional expert centers and systematic discussion of patients management at national tumor board. We reviewed our experience in stage III thymic tumors I norder to evaluate the value of tumor board recommendations and multidisciplinary approach.

Methods:We conducted a retrospective analysis of patients (pts) with stage III TET discussed at the RYTHMIC tumor board from January 2012 to December 2015.Clinical, pathologic and surgical data were prospectively collected in a central database. Survival rates were based on Kaplan-Meier estimation. Cox proportional hazard models were used to evaluate prognostic factors for disease free survival (DFS) and overall survival (OS).
Results: 150 pts were included in the analysis. Median age was 64 years [18 – 91], 56%males, thymoma A-B2/ B3-thymic carcinoma in 52% and 47% respectively; 12%presented with autoimmune disorder (76% myasthenia). Local treatment was surgery in 134 pts (90%) followed by radiotherapy (RT) in 90 pts; 26 pts received preoperative chemotherapy (CT). Complete resection rate (R0) was 53%. Among 38 pts considered on-surgical candidates at diagnosis, 26 pts became resectable after induction CT with a R0 rate of 58%; 12 pts received CT-RT and/or CT as primary treatment. Recurrence rate was 38% (n = 57), first sites were pleural (n = 32) and lung (n = 12). The 5-year OSand DFS were 88% and 32% respectively. Gender (p = 0.04), histology (p = 0.02) and surgery (p < 0.001) as primary treatment modality were significant prognostic factors for OS in multivariate analysis. Histology (p = 0.02) and adjuvant RT (p = 0.05) were significantly associated with DFS. Completeness of resection was not associated with survival in our cohort.
Conclusions: Surgery followed by radiotherapy improves outcome irrespectively of R0.Stage III TET not candidate to surgery should be reassessed for resection after induction chemotherapy.
Legal entity responsible for the study: N/A
Funding: RYTHMIC
Disclosure: All authors have declared no conflicts of interest.

1510PD Pathological central review of 400 thymic epithelial tumors(TET): The national network RYTHMIC experience

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Background: RYTHMIC (Réseau tumeurs THYMiques et Cancer) is a nationwidenetwork for TET appointed in 2012 by the French National Cancer Institute. The objectives of the network are management of clinical tumor board and centralpathologic review of all cases. RYTHMIC Tumor Board is based on initial histopathological diagnosis.
Methods: Pathological central review of patients diagnosed with TET from January2012 to May 2016 was made by a panel of 10 expert pathologists from the working group. Assessment of agreement or disagreement between the initial institution and the panel review was made according the WHO 2004/2015 and new ITMIG proposals for histologic typing and staging. Discordances were classified as "major" when they would have changed the therapy or management of patients according to the RYTHMIC guidelines.
Results: A total of 400 specimens were reviewed. Considering either histological subtype and/or staging, a total of 172 discordances in 157 patients (39%) were identified as follow: 111 concerning histological diagnosis and 61 regarding stage. A total of 31 major discordances in 29 patients (7%) were identified: 18 patients for whom post-surgical treatment recommendation concerning adjuvant radiotherapy would have been changed and 11 patients for whom management of disease should have been modified. The most frequent disagreement was the sub-diagnosis of stage III reflecting the underlying difficulty in pericardial and/or mediastinal pleura histological invasion. Additionally, major disagreement between the initial and panel pathology's stage and subsequent interpretation by the working group at national tumor board was found in 4 patients, enhancing the importance of an expert pathologist at the RYTHMIC network committee.
Conclusions: The RYTHMIC experience confirms the relevance of an expert histopathological panel diagnosis of thymic malignancies and for better decision-making in particular concerning post-operative radiotherapy to avoid over- or under-treatment of the patients.
Legal entity responsible for the study: N/A
Funding: RYTHMIC
Disclosure: All authors have declared no conflicts of interest.

ESMO Clinical Practice Guidelines session

Chronic lymphocytic leukaemia case presentation

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