588P Analysis and adherence to the ASCO recommendations for research biopsies and archival tissue requirements in clinical trials conducted at Institut Jules Bordet (IJB) from 2015 to 2019

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Background: Biomarkers in clinical trials as well as the need for correlative studies have led to the massive incorporation of research biopsies and archival tissue collection, with potentially risks and no direct benefit for patients. In 2019, ASCO has released an ethical framework (Levit LA et al. JCO 2019) to provide guidance on incorporating research biopsies in clinical trials.

Methods: We collected biopsy requirements of oncological clinical trials conducted at IJB between 2015 and 2019 to examine adherence with the ASCO Ethical Framework. We used logistic regression models to test the association between the request for biopsy, the request for tissue and the adherence to ASCO framework and some trials characteristics.

Results: Between January 2015 and December 2019, 178 studies were conducted at IJB. 138 (78%) were sponsored by industry, 132 (74%) were phase II and III studies and 141 (79%) involved metastatic disease. Tissue was required for inclusion, including archival tissue or new biopsy, for 119 (67%) studies. New biopsies were mandatory in 59 (33%) studies. Among those requesting more than one mandatory biopsy (N=25), 84% did not follow ASCO's framework. Additional characteristics of biopsies and informed consent documents are displayed in the table. In multivariate analysis, the request for tissue or new biopsies increased in early phase studies ($p<0.001$, $p<0.001$ respectively) and in studies investigating innovative treatments (immunotherapy or targeted therapies) ($p<0.01$, $p=0.02$). Compliance to ASCO framework decreased with time ($p<0.001$) and in early phase studies ($p<0.001$).

Table: 588P

	Studies requiring tissue (n=119)	Studies requiring mandatory biopsies (n=59)
Sponsor		
Academic	22 (18%)	9 (15%)
Industry	97 (82%)	50 (85%)
Early-phase studies	41 (34%)	29 (49%)
Number of mandatory biopsies		
0	60 (50%)	0
1	34 (29%)	34 (58%)
2	23 (19%)	23 (39%)
3	2 (2%)	2 (3%)
Biomarkers		
Expected utility: necessary for inclusion or primary objective	52 (44%)	19 (32%)
Potential utility: necessary for secondary objective	5 (4%)	4 (7%)
Unknown utility: necessary for exploratory objective	62 (52%)	36 (61%)
Adherence with ASCO Ethical Framework	80 (67%)	23 (39%)
Consent Characteristics		
Risk mentioned	66 (55%)	41 (70%)
Benefit mentioned	75 (63%)	38 (64%)

Conclusions: Numerous studies required tissue or new biopsies for exploratory objectives of unknown clinical utility. Request for tissue increases through years whereas compliance to ASCO's Framework decreases. Future studies should follow ASCO's Ethical Framework whose aim is to improve the ethics of research biopsies.

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589P The impact of sarcopenia in patients enrolled in early phase cancer trials

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Background: A good fitness level is required for patients (pts) wishing to enrol on most early phase cancer trials (EPCT). This is assessed by performance status and scoring systems such as the Royal Marsden Hospital (RMH) Score and MD Anderson Cancer Centre (MDACC) score. Reduced muscle mass (sarcopenia) as measured on CT scan at the level of L3 vertebrae is a prognostic biomarker for many cancers and may increase risk of drug toxicity. Our aim was to validate the RMH and MDACC scores in a cohort of Christie Hospital NHS Foundation Trust pts enrolled on early phase clinical trials and assess the impact of sarcopenia.

Methods: Retrospective case note review of pts data from 2014-2019, CT images taken from trial baseline and the L3 CT slice identified by the author. Demographics including age, gender, co-morbidities and prior treatment were collected. Software to delineate skeletal muscle from bone, fat and subcutaneous tissues was used to calculate skeletal muscle area, density (SMD) and skeletal muscle index (SMI). Dose modifying toxicity (DMT) defined as any drug-related cause of drug interruption or dose reduction.

Results: Full analysis including CT images was possible on 220/357 pts enrolled over 29 EPCTs. Pts omitted if on >1 trial or if no available imaging. Mean age 59 years, 58% of pts were female. Median RMH and MDACC scores were 1 (range 0-3 and 0-5), mean body mass index (BMI) 26.5 and sarcopenia was present in 17.27% of pts. RMH and MDACC scores correlated with poorer survival on univariate analysis ($p<0.001$) and with 90-day mortality (p 0.014 and 0.018 respectively) but not with DMTs (p 0.34 and 0.61 respectively). Sarcopenia was associated with poorer survival on log-rank analysis (p 0.043) and showed a trend towards significance on multivariate analysis (p 0.075) but not 90-day mortality (p 0.26), or DMT (p 0.36). On multivariate analysis reduced SMD approached significance (p0.054) and MDACC score and weight loss >3% were significantly associated with reduced survival (p 0.016 and 0.002).

Conclusions: The RMH and MDACC scores both demonstrated validity in our cohort. Fitness was good and rates of sarcopenia were low. RMH, MDACC scores and sarcopenia were not associated with DMTs in our cohort. However, despite low rates, pts with sarcopenia did have poorer survival outcomes.

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590P A double-blind, randomized, parallel group study to demonstrate the equivalent pharmacokinetic properties of a single intravenous dose HD201, a trastuzumab biosimilar candidate, versus EU trastuzumab and US trastuzumab

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Background: PharmaPrestige Co., Ltd. (Singapore) has developed HD201, a biosimilar candidate of the reference trastuzumab product. Among the stepwise approach to ensure comparability between the biosimilar candidate and the reference medical product, a phase I in healthy subjects is recommended to demonstrate the pharmacokinetic (PK) equivalence. We report the results of this phase I trial (NCT03776240).

Methods: The primary objective of the study was to demonstrate (PK) equivalence of HD201, EU-Herceptin®, and US-Herceptin® given at 6 mg/kg as a 90-minute i.v. infusion to healthy male subjects. A pairwise comparisons based on 3 co-primary