endpoints including AUC0–<inf>τ</inf>, C<inf>max</inf> and AUC0–<inf>τ</inf> were undertaken. PK equivalence was to be concluded if the 90% confidence interval for the ratio of geometric means for each criterion were within the conventional equivalence margin of 80% to 125%. Secondary objectives included assessment of other PK parameters, safety, tolerability, and immunogenicity in the 3 arms.

Results: A total of 105 healthy male subjects were randomized in this study. Pairwise comparisons for all PK criteria of judgements in all groups provided confident intervals included between the margins of equivalence. PK profiles including <sup>τ</sup>−<sub>max</sub>, <sup>C</sup>max, CI and <sup>T</sup>−<sub>max</sub> were similar across treatments. The frequency of subjects with adverse events of special interest was slightly lower in the HD201 group (20.0%) compared to the other treatment groups (EU-Herceptin: 34.3%; US-Herceptin: 31.4%). The commonest adverse events related to treatment were infusion related reactions and administration site reactions.

Conclusions: Overall, HD201 demonstrates equivalent PK to both EU-Herceptin® and US-Herceptin®. A large randomized study (TROIKA) aimed to demonstrate a similar activity in neoadjuvant setting for early breast cancer is ongoing (NCT03013504).

Legal entity responsible for the study: Prestige Pharma.

Funding: Prestige Pharma.


https://doi.org/10.1016/j.annonc.2020.08.704

591P Distress and perceived information among patients in phase I trials and their relatives: A prospective study


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Background: It is important to ensure equal access to and adequate understanding of study procedures in phase I trials. The trajectory of psychological distress associated with enrolment into phase I cancer trials and understanding of informed consent among patients and relatives in a phase I setting has not previously been investigated.

Methods: The association between levels of distress and later enrolment into phase I trial was investigated using a Cox regression model for referred patients (N=205). As the first study we investigated the understanding of informed consent among enrolled patients (N=46) and their relatives (N=35). The association between distress and understanding of informed consent was investigated using linear mixed-effects models.

Results: We identified no association with enrolment for a high level of stress compared to low (adjusted hazard ratio (HR), 1.8; 95% CI, 0.9 to 3.4); for mild symptoms of anxiety compared to minimal (HR, 1.2; 95% CI, 0.5 to 3.2); or for severe symptoms of anxiety compared to minimal (HR, 1.2; 95% CI, 0.5 to 3.2); or for mild symptoms of depression compared to minimal (HR, 0.8; 95% CI, 0.4 to 1.6). Patients’ and relatives’ understanding of informed consent in complex phase I trials was near the level reported for cancer trials in general, although some aspects were severe symptoms of anxiety compared to minimal (HR, 1.2; 95% CI, 0.5 to 3.2); or for mild symptoms of depression compared to minimal (HR, 0.8; 95% CI, 0.4 to 1.6).

Conclusions: Our results suggest that distress does not compromise enrolment or understanding of informed consent in phase I trials.

Legal entity responsible for the study: The authors.

Funding: A.P. Møller Foundation, Danish Cancer Society, and The Health Foundation.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.705

592P A predictive score of antitumour activity of novel agents in cancer patients treated in early phase studies

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Background: Antitumour activity is an important goal of Ph1 trials of INDs. We reviewed our series to find associations of RECIST response to baseline clinical variables and to define a predictive score.

Methods: We analyzed our pt treated in Ph1 trials, except ClinPharm, from Nov08 to Dec16. 28 baseline clinical (age, sex, ECOG, BMI, hypothyroid, HBP, DM, clots, RBC/lymph, WBC, TBil, Creat, GGT, LDH, ANC/lymph, PLT/lymph, Ca, Mg) values were collected; also objective response (OR), toxicity and therapy type. The variables associated to OR in the univariate analysis (U, p<0.05, chi-square test) were included in the step-wise logistic regression multivariate analysis (MA). The ones found to keep statistically significant were included in a predictive score of antitumour activity. Kaplan-Meier survival curves were compared with log-rank test. p values are 2-sided.

Results: 773 consecutive pt treated in 85 ph1 trials in START Madrid-CIOCC were included. Mean age was 58.7 y (range: 18-87); 48.1% were male. ECOG G: 55.8%; 1, 42.2%; 26% pt had GI tumours, 14% breast, and 12% GYN. 131 pt (17.3%) received IO, 303 (39.9%) targeted and 325 (42.8%) chemo drugs, and no statistically significant differences in OR rate or mOS were seen. 103 of 730 evaluable pt achieved an OR (14.1%), and 271 (48.8%) stable disease; their mOS was 10.8 m (95%CI: 9.8-10.8). The UA of the 28 variables showed that BMI≥25 kg/m<sup>2</sup> (p=0.18), <3 prior lines (p=0.001), normal AlkPhos (p=0.001), AST (p=0.033), GGT (p=0.021), and LDH (p=0.025), and ANC/lymph<sub>≤</sub>5 (p=0.047) were predictive of OR. Of these, BMI≥25 kg/m<sup>2</sup> (p=0.021), <3 prior lines (p=0.002) and normal AlkPhos (p=0.012) were found to be independent factors associated to OR in the MA. The presence of 0 to 3 altered factors was associated to worsening OS (X<sup>2</sup>, 18.1; p=0.001). A score of 0 vs. 2-3 unfavorable factors was predictive of OR (17% vs. 7.6%; X<sup>2</sup>, 11.9; p=0.003) and OS (11.6 m vs. 8.6 m; log rank, 7.8; p=0.005).

Conclusions: A high number of pt might derive clinical benefit (OR≥50, SL26%) from ph1 trials. A practical score based on BMI, <3 prior lines and AlkPhos (0-1 factors) was predictive of antitumour activity (OR, OS). If prospectively validated, it will help in pt selection.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.706

593P Longitudinal description of clinical trials for the development of cyclin-dependent kinases inhibitors


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Background: Drug development follows a progressive transition from preclinical studies to clinical practice across the multiple phases of clinical research. We aimed at describing the step-by-step evolution of a homogenous class of agents, cyclin-dependent kinases inhibitors, with a focus on phase (ph) I trials, a springboard for clinical development.

Methods: Trials registered on ClinicalTrials.gov were extracted using the following search parameters: palbociclib (P00332299; lbrance), ribociclib (LEED01; Kisquail), and abemaciclib (LY2835219; Verzenio), with a limit through the end of 2019.

Results: The analysis included 383 studies, conducted from 2004 to 2019, investigating palbociclib (53%), ribociclib (24%), abemaciclib (20%), or >1 of those drugs (3%). Trials were breast specific in 47% (181), non-breast in 53% (202); sponsored by industry in 38% (146), by a non-profit organization or academia in 30% (114), by their co-participation in 32% (123). A trend over time was registered in favour of breast specific studies (p=0.002) and academia involvement (p<0.0001). Overall, 125 trials were conducted for breast (33%), 40 (31%), 152 ph2 (40%), 3 ph2-3 (1%), 35 ph3 (9%), 7 ph4 (2%), 4 EAP (1%). In particular, among 125 ph1 trials, 30 enrolled healthy participants (24%), 30 enrolled patients with multiple solid tumours (24%), 30 breast (24%), 10 brain (8%) and 25 other tumour types (20%). Out of 125 ph1 studies, 75 (60%) were sponsored by industry, 22 (18%) by a non-profit organization or academia, 28 (22%) by their co-participation. The designated primary endpoint was dose limiting toxicity in 32 (26%), maximum tolerated dose in 24 (19%), recommended phase two dose in 4 (3%), and safety in 25 (20%) and in 8 cases (6%) a biological endpoint. The intervention assignment followed a crossover model in 16 (13%), parallel in 38 (30%), sequential in 9 (7%), single arm in the remnant 62 cases (49%).