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201P Afatinib for EGFR, HER2 or HER3 mutated solid tumors: A phase II Belgian precision study

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Background: The Belgian Precision initiative aims to implement tumor-agnostic NGS in advanced cancer patients (pts) and enhance access to genotype-matching drugs. The current study aimed to investigate the efficacy of afatinib in advanced pre-treated solid cancers with an EGFR (excluding non-small cell lung cancer (NSCLC)), HER2 or HER3 mutation.

Methods: Open-label phase 2 study including 3 cohorts for previously treated advanced cancers: EGFR, HER2 and HER3 mutated. The primary endpoint for each cohort was objective response rate (ORR). Response assessment was performed every 8 weeks. For each cohort, a Simon two-stage design was used. The null hypothesis that the true ORR is 10%, was tested against a one-sided alternative that the true ORR is 30%. If two or more ORR were observed in the first ten pts, 19 additional pts were included (type I error 5% and power 80%) Secondary endpoints were disease control rate (DCR), duration of response (DOR), progression-free survival (PFS), overall survival (OS) and safety.

Results: A total of 45 pts were included in the trial with median age 62 years. The EGFR cohort comprised 7 pts: 2 pancreas, 1 head and neck, 1 breast, 1 endocrine tumor, 1 cervix and 1 kidney. The HER2 cohort comprised 30 pts: 11 NSCLC, 8 breast, 3 cervix, 2 colorectal, 2 head and neck, 1 bladder, 1 kidney, 1 liver and 1 pancreas. The HER3 cohort comprised 8 pts: 2 breast, 2 pancreas, 1 colorectal, 1 head and neck, 1 esophagus and 1 stomach. ORR and DCR were respectively 28.6% and 42.9% in the EGFR cohort, 3% and 49% in the HER2 cohort and 0% and 62.5% in the HER3 cohort. Partial responses were observed in a HER2-mutated NSCLC (1/11) with a DOR of 8.5 months, an EGFR-mutated breast cancer (1/1) with a DOR of 6.6 months and an EGFR-mutated pancreas cancer (1/2) with a DOR of 15.4 months. PFS and OS data will be presented at the meeting Safety data were consistent with the known safety profile of afatinib.

Conclusions: Although three pts demonstrated a clinical meaningful benefit, afatinib did not result in a significant ORR improvement in the HER2 cohort, which completed accrual. Recruitment was hampered by a lack of systematic agnostic NGS sequencing and the COVID epidemic. Broader and more systematic agnostic NGS would enable further exploration of HER inhibition in solid tumors

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202P Participant perceptions and mammography adherence from DETECT-A: The first prospective interventional trial of a multi-cancer early detection (MCED) blood test

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Background: MCED tests may improve early cancer detection, but the impact of MCED testing on anxiety and standard of care (SOC) screening adherence is unknown. The DETECT-A trial evaluated the CancerSEEK MCED test in 9,911 women without a cancer history (Science, 359:6499, 2020). DETECT-A participants without a cancer diagnosis were invited to a follow-up observational study involving annual surveys. Here we report on participant satisfaction, anxiety, intent to adhere to SOC cancer screening, and adherence to breast cancer screening.

Methods: The survey, conducted approximately 3 years after DETECT-A enrollment, assessed: a) whether participants regretted DETECT-A participation or would participate again, b) how likely they were to adhere to routine cancer screenings, and c) how participation affected their anxiety. Adherence to biennial mammography screening was assessed at the month of survey completion for screening-eligible participants with evaluable medical records.

Results: Of the 7573 DETECT-A participants contacted, 3,870 (51%) completed a survey. Of the 3,788 respondents who answered all survey questions, 96.9% indicated no participation regret, 98.8% would participate again, 99.5% reported being equally or more likely to adhere to SOC screening, and 98.7% reported no change in or reduced anxiety. Of 1,053 participants eligible for mammography with available health records, 93.4% (n=984) were adherent with mammography screening. 94.3% of participants with false positive (FP) results who completed a survey ($n = 35$) reported no change or a reduction in anxiety; 5.7% (95%CI 1.6%-18.6%) reported an increase in anxiety compared to 1.3% (95% CI 0.9%-1.7%) of participants with true negative results ($p = 0.07$).

Conclusions: A follow-up study of MCED participant survey responses revealed high levels of participant satisfaction, intent to adhere to SOC screening, and mammography adherence. Most participants reported no change or a decrease in anxiety. This data suggest that MCED testing with imaging-based diagnostic resolution does not significantly increase anxiety or negatively impact mammography adherence for most participants, including those with FP results.

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