26 VALIDATION OF THE PRIMARY IMMUNE RESPONSE (PIR) TEST IN ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC): BLINDED RETROSPECTIVE ANALYSES FROM THE POPLAR AND OAK TRIALS

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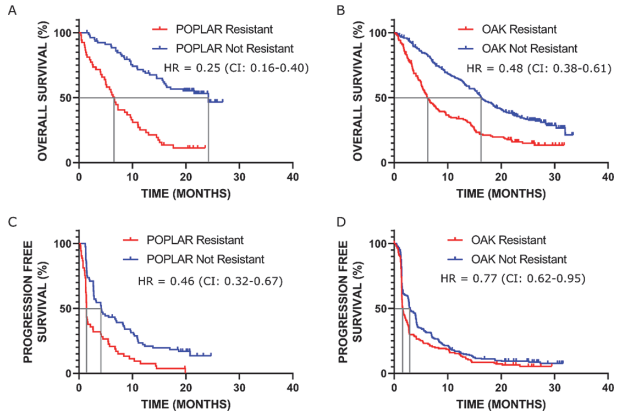
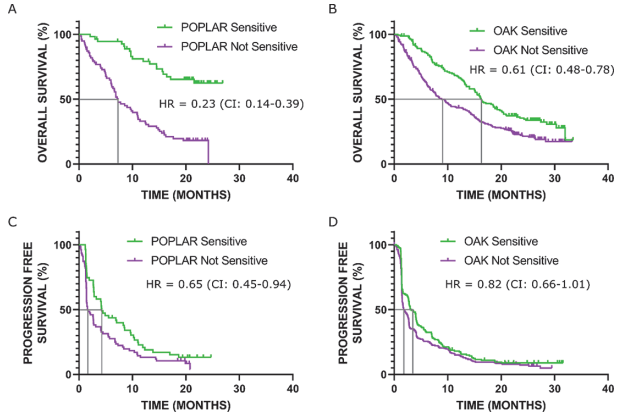
Background Biomarkers of immune checkpoint inhibitor (ICI) efficacy can be used for patient selection. PD-L1 expression in tumor tissue is used to determine eligibility for combination or monotherapy in 1st line NSCLC.[1, 2] The liquid-biopsy mass spectrometry-based PIR test was developed to capture the role of patient biology on ICI outcomes.[3] The test, stratifying patients into Resistant, Intermediate, and Sensitive groups, was associated with outcome on nivolumab treatment in 2nd line NSCLC patients.[3] In this study, we blind validated PIR classifications in two large clinical studies (POPLAR[4] and OAK[5]) of advanced NSCLC patients treated in the second or third line with atezolizumab.



Abstract 23 Figure 1 Kaplan-Meier plots of OS and PFS by test classification Resistant vs Not Resistant for the POPLAR and OAK cohorts



Abstract 23 Figure 2 Kaplan-Meier plots of OS and PFS by test classification Not Sensitive vs Sensitive for the POPLAR and OAK cohorts

Methods Pretreatment serum samples from patients assigned to receive atezolizumab in the two studies (POPLAR (NCT01903993) and OAK (NCT02008227)) underwent PIR testing blinded to all clinical data. Association of test classification, as Sensitive vs Not Sensitive (Resistant+Intermediate) and Resistant vs Not Resistant (Sensitive+Intermediate), with overall survival (OS) and progression-free survival (PFS) was investigated using Cox proportion hazards models in univariate and multivariate analysis.

Results PIR classifications were generated for 133 (POPLAR) and 403 (OAK) samples; the remaining available samples failed test QC, mainly due to hemolysis. PIR classified the POPLAR samples as 53 (40%) Resistant, 25 (19%) Intermediate, 55 (41%) Sensitive and the OAK samples as 154 (38%) Resistant, 89 (22%) Intermediate, and 160 (40%) Sensitive. In both cohorts, OS and PFS were better in the Not Resistant vs Resistant group (figure 1). OS and PFS were superior in the Sensitive vs Not Sensitive group in the POPLAR cohort, while OS was better and PFS showed indications of superiority in the OAK cohort (figure 2). Multivariate analysis within the OAK cohort showed that test classification predicted OS when adjusted for baseline factors, including PD-L1 negative vs positive, with hazard ratio 0.51 (95% confidence interval (CI) 0.40–0.65) for Resistant vs Not Resistant and 0.65 (CI: 0.50–0.83) for Sensitive vs Not Sensitive.

Conclusions The PIR test stratified outcomes for patients treated with atezolizumab in second and third line NSCLC even when adjusted for PD-L1 expression. The combination of both tumor and host biomarkers appears to provide a more specific prognosis of NSCLC treated with ICIs.

Trial Registration clinicaltrials.gov NCT01903993 and NCT02008227

REFERENCES

1. Roy S Herbst, Giuseppe Giaccone, Filippo de Marinis et al. Atezolizumab for first-line treatment of PD-L1-selected patients with NSCLC. *N Engl J Med* 2020 Oct 1;**383**(14):1328–1339
2. Tony S K Mok, Yi-Long Wu, Iveta Kudaba et al. Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled, phase 3 trial. *Lancet* 2019 May 4;**393**(10183):1819–1830.
3. Muller M, Hummelink K, Hurkmans D, et al. A serum protein classifier identifying patients with advanced non-small cell lung cancer who derive clinical benefit from treatment with immune checkpoint inhibitors. *Clin Cancer Res* 2020;**26**(19):5188–5197.
4. Fehrenbacher L, Spira A, Ballinger M, et al. Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): a multicentre, open-label, phase 2 randomised controlled trial. *Lancet* 2016;**387**(10030):1837–1846.
5. Rittmeyer A, Barlesi F, Waterkamp D, et al. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicenter randomized controlled trial. *Lancet* 2017;**389**(10066):255–265.

Ethics Approval The OAK study was done in 194 academic medical centers and community oncology practices across 31 countries worldwide. The study was done in full accordance with the guidelines for Good Clinical Practice and the Declaration of Helsinki. All patients gave written informed consent. The POPLAR trial was done at 61 academic medical centers

and community oncology practices across 13 countries in Europe and North America. The study was done in full accordance with the guidelines for Good Clinical Practice and the Declaration of Helsinki. Protocol (and modification) approval was obtained from an independent ethics committee for each site. Patients gave written informed consent.

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