

PAN-TUMOR HARMONIZATION OF PATHOLOGIC RESPONSE ASSESSMENT FOR STANDARDIZED DATA COLLECTION IN NEOADJUVANT IO TRIALS (PATHDATA): INTERIM ANALYSIS OF A MULTI-INSTITUTIONAL REPRODUCIBILITY STUDY

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Background Immunotherapeutic agents are now being investigated for treating earlier-stage cancers. Radiographic assessment by RECIST, widely used to assess treatment response in clinical trials for advanced cancers, has limitations in the neoadjuvant setting; and pathologic response assessment is increasingly being used as a primary and/or secondary endpoint. To that end, a pan-tumor scoring system for assessing pathologic response was developed.^{1, 2} This scoring system allows for the quantitative assessment of residual viable tumor (RVT) in multiple locations: i.e. primary and lymph node (LN) or distant metastases, akin to RECIST.%RVT scored using this system been associated with patient outcomes after treatment with anti-PD-1-based therapies. Additionally,%RVT in LN has been shown to have additive value to %RVT in the primary tumor when predicting patient survival.³ As a result, pathologists are now being asked to score pathologic response in the primary tumor and LN as a part of ongoing clinical trials and routine clinical care. Here, we evaluated the reproducibility of %RVT scoring using pan-tumor immune-related pathologic response criteria (irPRC).

Methods A multi-institutional, international study led by the Society for Immunotherapy of Cancer was initiated to assess the concordance of pathologic response assessment in resection specimens from patients treated with anti-PD-1-based therapies. Online lecture-based modules for irPRC scoring were developed, and 14 pathologists from multiple institutions, including academic and industry partners, were trained to score H&E-stained slides. To date, the pathologists have scored n=15 pathology cases (of a planned 30) from resection specimens from >10 different tumor types, in part derived from phase II/III clinical trials.%RVT in the primary tumor and LN from patient specimens were scored separately (n=18 individual specimens with a total of 236 slides scored to date by each pathologist).

Results High reproducibility amongst pathologists was observed using irPRC scoring (overall intraclass correlation coefficient, ICC [95% Confidence Interval]: 0.88 [0.79–0.94]. In subset analysis, similar reproducibility was seen for the primary tumor and LN, primary tumor ICC =0.88 [0.76–0.96] and LN ICC =0.88 [0.76–0.97].

Conclusions At the first interim analysis, scoring of pathologic response using irPRC appears highly reproducible, irrespective

of disease location (i.e. primary tumor vs lymph node metastasis). Future analyses will include subset analyses by tumor type. A post-study survey completed by the participating pathologists will be used to refine irPRC training materials prior to dissemination to the wider immuno-oncology community.

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Ethics Approval This study was approved by the Johns Hopkins University Institutional Review Board.

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