MAJOR PATHOLOGIC RESPONSE AFTER A SINGLE RADIOTHERAPY FRACTION + A SINGLE PEMBROLIZUMAB DOSE GIVEN PREOPERATIVELY IN PATIENTS WITH cT1N0 TRIPLE NEGATIVE BREAST CANCER (TNBC) – PRELIMINARY RESULTS OF A PHASE 1B/2 STUDY (NCT04454528)

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Background Pembrolizumab (Pembro) was recently approved for use in combination with neoadjuvant chemotherapy for the treatment of cT2-4N0-2 or T1cN1-2 triple negative breast cancer (TNBC). For patients with early stage (e.g. cT1N0) disease, this regimen may be excessive. We hypothesize that a single 7 Gy radiotherapy (RT) fraction directed at the tumor combined with a single Pembro dose given preoperatively (preop) in patients with early stage breast cancer is feasible and may result in pathologic response.

Methods Patients with cT1N0 TNBC or other subtypes and without a history of ipsilateral breast/chest wall RT or conditions that preclude Pembro treatment are eligible to enroll in this 21-day window of opportunity 3-armed study. Patients either receive RT, Pembro, then surgery; or Pembro, RT, then surgery; or Pembro only in arm 1, 2, or 3, respectively. The primary endpoints were feasibility and tolerability. The secondary endpoints were % change in tumor infiltrating lymphocytes (TILs) and pathologic response. A major pathologic response is defined as <10% residual invasive tumor in post-treatment resected tissues. All patients underwent standard of care adjuvant therapy following surgery.

Results Patients’ clinical characteristics are summarized in Table 1. An initial 6 patients (phase 1b; 4 in arm 1 and 2 in arm 2) completed preop treatment with none experiencing >grade 2 skin toxicity or surgery delay (defined as >14 days), thus establishing feasibility. Study is expanded to phase 2 in which patients are assigned 1:1:1 into arms 1, 2, and 3 according to subtype. Comparison of pre- and post-treatment tissues demonstrated that ΔTILs increased significantly in TNBC (21 ±15%, n=9) than in other subtypes (1±2%, n=3), p=0.049. Major pathologic response (PR) was observed in 3 of 9 TNBC (33%) (2 in arm 1; 1 in arm 2) including 1 with complete PR (arm 1).

Conclusions For the first time to our knowledge, a major PR was observed in TNBC after a single RT + 1 Pembro infusion given preop. Comprehensive digital spatial profiling of the pre- and post-treatment tumor microenvironment to identify potential biomarkers associated with PR is underway. Results of this proof-of-concept study may provide the rationale to evaluate the effectiveness of de-escalating preoperative combination immunotherapy in select patients in future studies.

Trial Registration NCT04454528

REFERENCES