in patients with aggressive recurrent primary brain tumors. Our preclinical data show that Chemokine modulating (CKM) regimen [rintatolimod, interferon (IFN)-α2b and COX-2 inhibitor] also selectively attracts effector CTLs and Th1 cells (but not suppressive regulatory T-cells or myeloid-derived suppressor cells) into tumors. Importantly, CKM preferentially promotes CTL migration into tumor rather than healthy tissues, providing rationale for its systemic use. We hypothesize that anti-HER2/3 type 1 polarized DC1s in combination with CKM and anti-PD1 will result in improved Th1/CTL response against HER2/3 epitopes, reduce brain recurrence and systemic progression.

Methods This is a phase II single-arm, non-randomized multicenter study (NCT04348747). Eligibility includes patients with triple negative and HER2+ BMBC ≥ 18 years, ECOG PS ≤ 1, normal marrow and organ function with asymptomatic untreated brain metastases who receive αDC1 q2 weeks x 3, with CKM [200 mg IV rintatolimod, IFN-α 20 million units/ m2 IV, celecoxib 200 mg oral BID] on days 1-3 with second and third dose of αDC1, followed by pembrolizumab 200 mg IV. Thereafter, pembrolizumab is given every 3 weeks, along with αDC1 and CKM every 3 months as booster dose until disease progression, intolerable side effects or withdrawal from study, or up to 24 months. Baseline and 3-week post-CKM treatment peripheral (non-CNS) biopsies are required for six patients. Primary objective is CNS response rate (RR) using RANO-BM criteria. If no CNS response is observed after 12 patients, study will be terminated. If ≥ 1 response observed, then 9 more patients will be enrolled, for a total of 21 patients. If ≥ 3 CR observed, the proposed therapy will be considered promising for further study. Secondary objectives include non-CNS RR per RECIST v1.1, median CNS, non-CNS and overall progression-free survival, overall survival and safety. Analysis of change in intratumoral biomarkers is an exploratory objective.

Results N/A

Conclusions N/A

Trial Registration NCT04348747

Ethics Approval The study was approved by Roswell Park Comprehensive Cancer Center Institution’s Ethics Board, approval number I-19-04120.

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321 PHASE I CLINICAL TRIAL ASSESSING THE COMBINATION OF SYSTEMIC CHEMOKINE MODULATORY REGIMEN TARGETING TLRI WITH NEOADJUVANT CHEMOTHERAPY IN TRIPLE NEGATIVE BREAST CANCER

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Background Neoadjuvant chemotherapy (NAC) with taxanes is the standard of care in triple negative breast cancer (TNBC). Intratumoral prevalence of CD8+ cytotoxic T-lymphocytes (CTLs) is associated with an improvement in relapse-free survival (RFS) and overall survival (OS), while regulatory T-cells (Treg) and myeloid derived suppressor cells (MDSC) are associated with poor survival. Higher ratio of CTL/Treg is associated with higher probability of obtaining pathological complete response (pCR), a surrogate marker for RFS. Intratumoral production of CCL5, CXCL9, CXCL10 and CXCL11 is critical for local infiltration with CTLs, while CCL2 is responsible for Treg attraction. Previous studies have shown that CXCL9 expression in the pre-treatment breast tissue is associated with a three-fold higher rate of achieving pCR. Our preclinical data show that Chemokine modulating (CKM) regimen, combining rintatolimod (TLR3 agonist), interferon (IFN)-α2b, and celecoxib (COX-2 inhibitor) increases CTL-attracting, and decreases MDSC-, Treg-favoring chemokines, increasing CTL/Treg ratio in tumor microenvironment, with preferential tumor tissue activation than adjacent healthy tissues. We hypothesize that the combination of CKM with paclitaxel will result in infiltration of TNBC with CTLs, and along with doxorubicin/cyclophosphamide (AC), result in higher pCR, translating into improved RFS and OS.

Methods In this phase I study NCT04081389, eligibility includes age ≥ 18 years, confirmed resectable TNBC, radiographically measurable disease ≥ 1 cm, ECOG PS ≤ 2, adequate organ and marrow function. Patients with autoimmune disease, serious mood disorders, invasive carcinoma within 3 years, history of peptic ulcers or hypersensitivity to NSAIDs will be excluded. We plan to treat three patients with early stage TNBC with paclitaxel 80 mg/m2 IV weekly for 12 weeks, rintatolimod 200 mg IV, celecoxib 200 mg oral twice daily, and accelerated titration of IFN-α2b at doses 0, 5, or 10 million units (MU)/m2 [Dose Levels (DL) 1, 2 and 3 respectively] on days 1–3 (no intra-patient dose escalation) in weeks 1–3. Dose-limiting toxicity (DLT) is defined as grade 3 or higher toxicities within the first 3 weeks. Any DLT will mandate recruitment per the 3+3 model. If no DLT, three patients will be enrolled at DL 4 at 20 MU/m2 IFN-α2b. This will be followed by standard dose-dense AC, and then surgery. The primary endpoint is safety and tolerability of combination and to identify the appropriate DL of CKM and paclitaxel for extended efficacy study. The secondary endpoints include investigation of efficacy (pCR and breast MRI response), along with RFS and OS. Intratumoral biomarkers will be analyzed in an exploratory manner.

Results N/A

Conclusions N/A

Trial Registration NCT04081389

Ethics Approval The study was approved by Roswell Park Comprehensive Cancer Center Institution’s Ethics Board, approval number I-73718.

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322 EFFICACY AND SAFETY OF GX-I7 PLUS PEMBROLIZUMAB FOR HEAVILY PRETREATED PATIENTS WITH METASTATIC TRIPLE NEGATIVE BREAST CANCER: THE PHASE 1B/2 KEYNOTE-899 STUDY

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Background Pembrolizumab monotherapy showed 9.6% ORR and did not significantly improve OS as 2L or 3L treatment for mTNBC compared to standard chemotherapy in phase 3 study (KEYNOTE-119) leading to high unmet needs of a new drug that could enhance the activity of pembrolizumab