

inclusion until the day preceding surgery (maximum 28 days therapy). The primary study outcome is to evaluate safety and tolerability of MRx0518 monotherapy in treatment naïve patients. Additional exploratory outcomes including identifying surrogate biomarkers of efficacy, microbiome analysis, effect on metabonomic markers and identification of histological and genomic alterations in paired pre-treatment (diagnostic biopsy) and post-treatment (surgical specimen) samples.

Results In part A, 17 patients received treatment, across tumour groups including breast (n=8), prostate (n=4), uterine (n=3), melanoma (n=1) and bladder (n=1). MRx0518 was well tolerated by all, with no grade 3/4 CTCAE toxicity reported, no severe adverse effects or treatment discontinuations. All patients proceeded to surgery, however the COVID-19 pandemic delayed surgery in 3 cases.

Analysis of the first 5* patient paired samples utilising the NanoString Pan Cancer IO 360TM Gene Expression panel has demonstrated significant changes in gene expression profiles in 48 genes (p

Conclusions This study has demonstrated the safety and tolerability of the live biotherapeutic MRx0518 in treatment naïve cancer patients. Exploratory analyses of post-treatment samples has echoed preclinical observations of increased infiltration of immune cells following treatment and will undergo further validation. Part B will focus on investigating efficacy in a further 100 treatment naïve patients with a placebo-controlled arm.

Trial Registration NCT03934827

Ethics Approval The study was approved by East of England - Cambridge East Research Ethics Committee approval number 18/EE/0091

REFERENCE

1. Lauté-Caly DL, Raftis EJ, Cowie P, *et al.* The flagellin of candidate live biotherapeutic *Enterococcus gallinarum* MRx0518 is a potent immunostimulant. *Scientific Reports* 2019;**9**(1):1-14. doi:10.1038/s41598-018-36926-8

*Data analysis has been censored at 18/9/2020, further samples analysis is ongoing and will be updated.

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CHANGES IN T CELL CLONALITY IN AWARE-1 STUDY, A WINDOW-OF-OPPORTUNITY STUDY WITH ATEZOLIZUMAB AND THE ONCOLYTIC VIRUS PELAREOREP IN EARLY BREAST CANCER

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Background A previous phase 2 study in metastatic breast cancer demonstrated a statistically significant improvement in overall survival (OS) in patients treated with pelareorep (pela) in combination with paclitaxel (PTX) versus PTX alone.¹ Given that pela is an intravenously delivered immuno-oncolytic reovirus, we hypothesized that the OS benefit from pela + PTX may be attributed to an adaptive T cell response triggered by pela. To examine if pela can mediate the priming of an anti-tumor immune response, we are conducting together with the SOLTI group the AWARE-1 study (a window-of-opportunity study of pela in early breast cancer), which is currently enrolling and for which initial translational research results are presented.

Methods AWARE-1 is a window-of-opportunity study to evaluate the safety and effect of pela ± atezolizumab on the tumor microenvironment (TME) in 38 women with early breast cancer. Patients are treated with pela on days 1, 2, 8, and 9, while atezolizumab is administered on day 3. Tumor biopsies are collected at diagnosis, day 3, and day ~21. Five cohorts will be examined: Cohort 1: HR+/HER2-neg (10 patients) receiving pelareorep + letrozole; Cohort 2: HR+/HER2-neg (10 patients) receiving pelareorep + letrozole + atezolizumab; Cohort 3: TNBC (6 patients) receiving pelareorep + atezolizumab; Cohort 4: HER2+/HR+ (6 patients) receiving pelareorep + trastuzumab + atezolizumab; Cohort 5: HER2+/HR- (6 patients) receiving pelareorep + trastuzumab + atezolizumab. The primary endpoint of the study is CelTIL score [2], a metric for quantifying the changes in tumor cellularity and infiltration of TILs, where an increase in CelTIL is associated with a favorable response to treatment. Tumor tissue is being examined for pela replication, and changes to the TME are being assessed by immunohistochemistry and T cell receptor sequencing (TCR-seq). Peripheral blood is also being examined by TCR-seq.

Results Detailed TCR-seq results from peripheral blood and tumor tissue are presented for the ten-patients enrolled into Cohort 1 who received pela and letrozole. In tumor tissue, T cell clonality increased in day 21 biopsies relative to baseline biopsies, with similar increases in T cell fraction (the number of T cells) in the majority of patients. In general, most of the tissue-expanded T cell clones were also seen in the peripheral blood.

Conclusions Overall, these preliminary data from cohort 1 of AWARE-1 demonstrate that pela mediates priming of a T cell-based immune response that occurs both systemically and within breast cancer tissue.

Trial Registration NCT04102618

Ethics Approval This study was approved by the Spanish Health Authority, protocol number 2018-003345-42.

REFERENCES

1. Bernstein V, *et al.* A randomized phase II study of weekly paclitaxel with or without pelareorep in patients with metastatic breast cancer: final analysis of Canadian Cancer Trials Group IND.213. *Breast Cancer Res Treat* 2018;**167**(2):485-493.
2. Nuciforo P, *et al.* A predictive model of pathologic response based on tumor cellularity and tumor-infiltrating lymphocytes (CelTIL) in HER2-positive breast cancer treated with chemo-free dual HER2 blockade. *Ann Oncol* 2018;**29**(1):170-177.

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