cancers, but with variable efficacy. Prior research has also suggested that systemic antibiotic (ABX) exposure may impact the intestinal microbiota and result in suboptimal ICI treatment outcomes. Our team published a systematic review and meta-analysis showing that ABX use could indeed decrease the survival of patients diagnosed with non-small-cell lung cancer (NSCLC) and treated with ICIs.[1] The present abstract aims at updating this meta-analysis by incorporating new studies that have been published in the period ranging from September 2019 to August 2020.

Methods Medline (through PubMed), the Cochrane Library and major oncology conferences proceedings were systematically searched to identify studies assessing the impact of ABX use on the clinical outcomes of NSCLC patients treated with ICIs. Studies were found eligible for inclusion when they mentioned a hazard ratio (HR) or Kaplan–Meier curves for overall survival (OS) or progression-free survival (PFS) based on antibiotic exposure. Pooled HRs for OS and PFS and HRs for OS and PFS according to different time windows for ABX exposure were calculated.

Results 6 eligible new studies were identified between September 2019 and August 2020 while 3 other studies were updated with new information. Altogether, 27 studies reported data for OS (6,436 patients, 826 of whom coming from new studies) and 24 for PFS (3,751 patients, 786 of whom coming from new studies). The pooled HR was 1.75 (95% confidence interval [CI]: 1.38–2.23) for OS and 1.57 (95% CI: 1.28–1.92) for PFS, confirming a significantly reduced survival in patients with NSCLC exposed to ABX. The detailed analysis in subgroups based on the time window of exposure (figure 1, figure 2) suggests that the deleterious effect of ABX is stronger when the exposition happens shortly before and after the initiation of the ICI treatment.

Conclusions The update of the meta-analysis confirms the previously reported deleterious effect of ABX on ICI treatment outcomes, taking into account the latest publications in the field. The topic deserves further research to uncover if the effect will stand with 1st line use of ICI together with chemotherapies and/or other approved combinations, elucidate the mechanisms at stake and improve care of patients.

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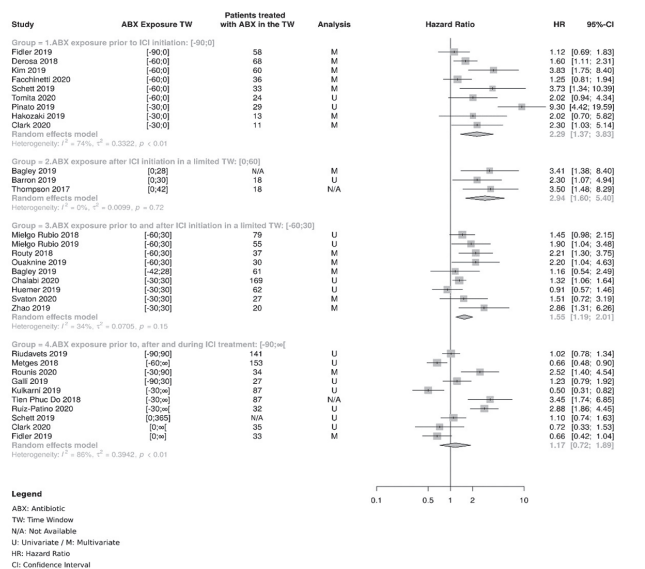
Abstract 671 Figure 1 Forest plot of hazard ratios for overall survival of patients diagnosed with NSCLC and exposed to antibiotics versus not exposed to antibiotics, according to the time window of antibiotic exposure
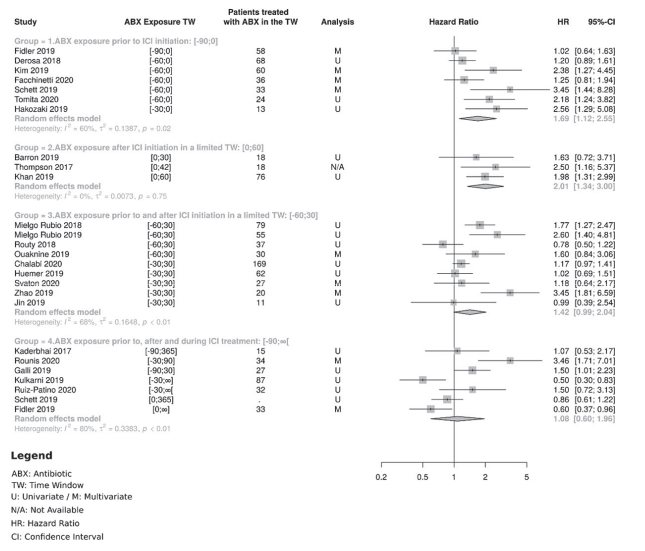
Abstract 671 Figure 2 Forest plot of hazard ratios for progression-free survival of patients diagnosed with NSCLC and exposed to antibiotics versus not exposed to antibiotics, according to the time window of antibiotic exposure

672   **IDENTIFICATION OF MICROBIAL-DERIVED HLA-BOUND PEPTIDES IN MELANOMA**

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Background The query for tumor shared and neo-antigens as a therapeutic approach has been the focus of cancer immunology for the past two decades. Notably, these peptide sequences can bind to HLA molecules and present on the cell surface, subsequently to be recognized by T-cell receptors (TCRs), activating the immune system and so facilitating in tumor rejection.[1–3] The search for new origins of targetable types of HLA peptides is consistently growing, and new studies show peptides that are derived from non-canonical open reading frames (ORFs), altered translation, proteasome splicing, viral proteins and more.[4–6] In light of the new findings, showing the important role of intra-tumor and gut bacteria in tumor-genesis and their effect on the immune response,[7–10] we went on a quest for discovering whether intracellular bacteria antigens can be presented by tumor cells, and whether these antigens may elicit an immune response.

Methods Combination of HLA peptidomics with 16S rDNA sequencing.

Results Combination of HLA peptidomics with 16S rDNA sequencing of 17 melanoma metastasis derived from 9 different patients, lead us to the unbiased identification of an intracellular bacterial peptide repertoire presented on HLA-I and HLA-II molecules. We were able to validate these results by co-culturing the bacterial species identified by 16S sequencing with the patient derived melanoma cells, further validating the peptide's presentation by preforming HLA peptidomics on the infected cells. Importantly, we were able to identify common bacterial peptides from different metastases of the same patient as well as from different patients. Some of the common bacterial peptides, as well as others, were able to elicit an immune response by the autologous tumor infiltrating lymphocytes (TILs), suggesting potential therapeutic implications of these peptides.

Conclusions The insights gathered through this study elucidate the effect of intra-tumor bacteria on the immune response and so, may lead to the development of novel clinical applications.

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673 | PRECISION MICROBIOME MAPPING IDENTIFIES A MICROBIOME SIGNATURE PREDICTIVE OF IMMUNE CHECKPOINT INHIBITOR RESPONSE ACROSS MULTIPLE RESEARCH STUDY COHORTS

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Background The gut microbiome of cancer patients appears to be associated with response to Immune Checkpoint Inhibitor (ICIs) treatment.[1–4] However, the bacteria linked to response differ between published studies.

Methods Longitudinal stool samples were collected from 69 patients with advanced melanoma receiving approved ICIs in the Cambridge (UK) MELRESIST study. Pretreatment samples were analysed by Microbiotica, using shotgun metagenomic sequencing. Microbiotica's sequencing platform comprises the world's leading Reference Genome Database and advanced Microbiome Bioinformatics to give the most comprehensive and precise mapping of the gut microbiome. This has enabled us to identify gut bacteria associated with ICI response missed using public reference genomes. Published microbiome studies in advanced melanoma,[1–3] renal cell carcinoma (RCC) and non-small cell lung cancer (NSCLC)[4] were reanalysed with the same platform.

Results Analysis of the MELRESIST samples showed an overall change in the microbiome composition between advanced melanoma patients and a panel of healthy donor samples, but not between patients who subsequently responded or did not respond to ICIs. However, we did identify a discrete microbiome signature which correlated with response. This signature predicted response with an accuracy of 93% in the MELRESIST cohort, but was less predictive in the published melanoma cohorts.[1–3] Therefore, we developed a bioinformatic analytical model, incorporating an interactive random forest model and the MELRESIST dataset, to identify a microbiome signature which was consistent across all published melanoma studies. This model was validated three times by accurately predicting the outcome of an independent cohort. A final microbiome signature was defined using the validated model on MELRESIST and the three published melanoma cohorts. This was very accurate at predicting response in all four studies combined (91%), or individually (82–100%). This signature was also predictive of response in a NSCLC study and to a lesser extent in RCC. The core of this signature is nine bacteria significantly increased in abundance in responders.

Conclusions Analysis of the MELRESIST study samples, precision microbiome profiling by the Microbiotica Platform and a validated bioinformatic analysis, have enabled us to identify a unique microbiome signature predictive of response to ICI therapy in four independent melanoma studies. This removes the challenge to the field of different bacteria apparently being associated with response in different studies, and could represent a new microbiome biomarker with clinical application. Nine core bacteria may be driving response and hold potential for co-therapy with ICIs.

Ethics Approval The study was approved by Newcastle & North Tyneside 2 Research Ethics Committee, approval number 11/NE/0312.

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674 | LATE ANTIBIOTIC ADMINISTRATION DURING DURVALUMAB TREATMENT MAY BE ASSOCIATED WITH CLINICAL BENEFIT

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Background Early concurrent antibiotic usage in patients receiving immune checkpoint inhibitors (ICIs) is linked to