

Update of a Systematic Review and Meta-Analysis Studying the Association Between Antibiotic Use and Clinical Outcomes of Non-Small-Cell Lung Cancer Patients Treated with Immune Checkpoint Inhibitors

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BACKGROUND

- Experimental studies involving mouse tumor models and fecal microbiota transplant from cancer patients have suggested that intestinal dysbiosis impacts the response to anti-PD(L1) mAb^{1,2,3}.
- Prior clinical research has strongly suggested that systemic antibiotic (ABX) exposure impacts the intestinal microbiota and may result in suboptimal immune checkpoint inhibitor (ICI) treatment outcomes.
- Our team published in March 2020 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 ICI⁴.
- Since the last literature screening in September 2019, new studies have been published on the topic, justifying an update of the meta-analysis.

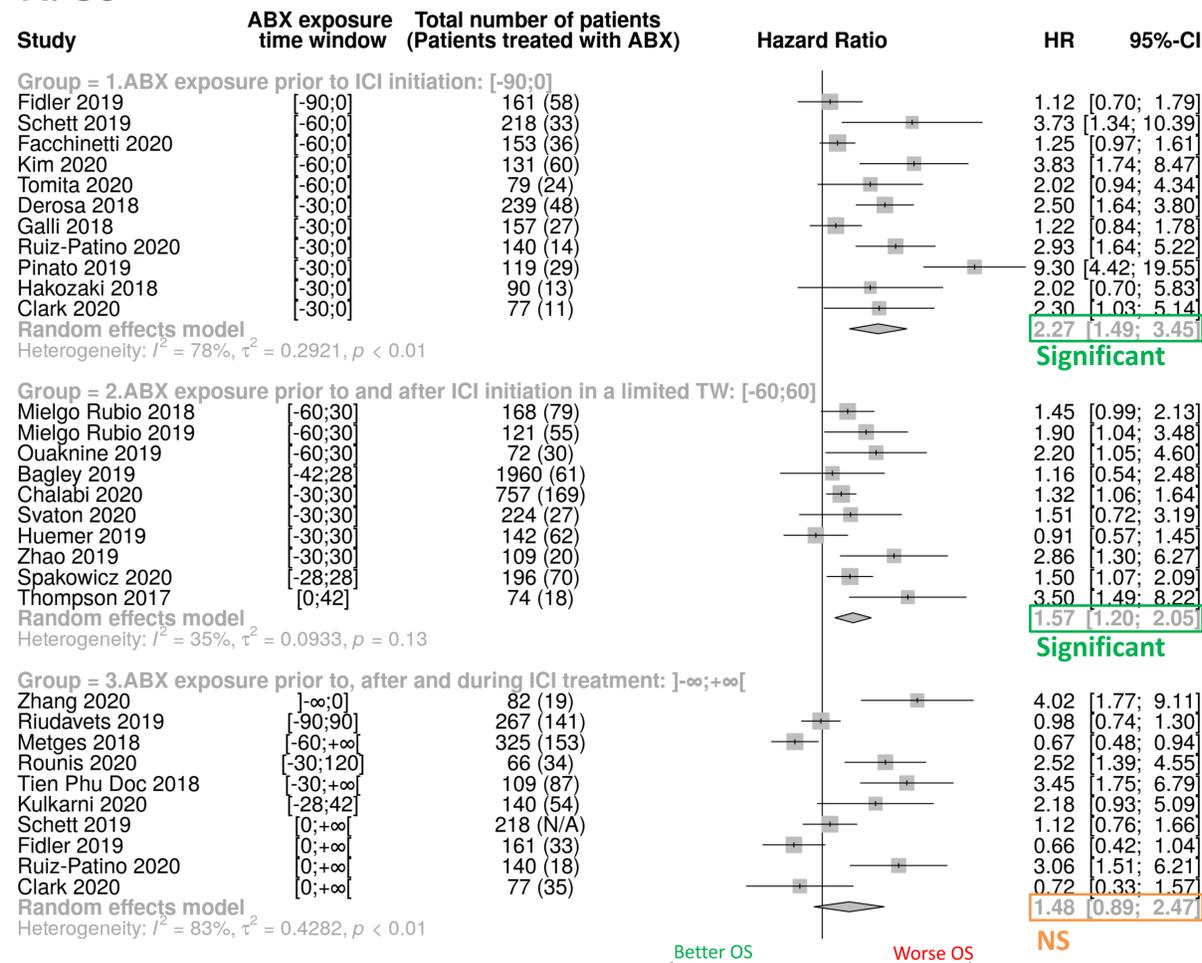
METHODS

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

RESULTS

27 studies reported data for OS (6,376 patients) and 22 for PFS (3,471 patients). The pooled HR was 1.73 (95% confidence interval [CI]: 1.38-2.17) for OS and 1.55 (95% CI: 1.27-1.90) 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) suggests that the deleterious effect of ABX is stronger when the exposition happens shortly before and after the start of the ICI treatment.

A: OS



B: PFS

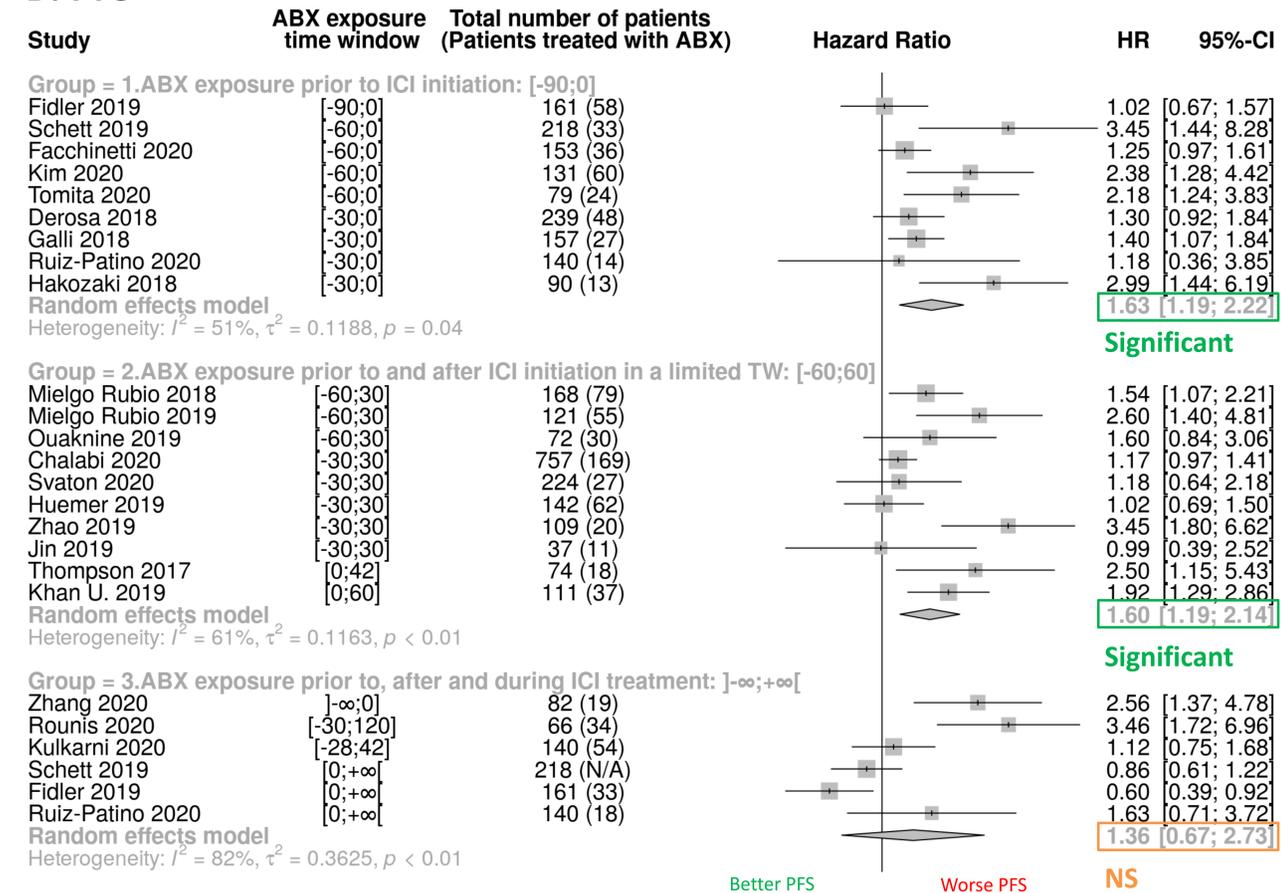


Figure 1: Forest plots of hazard ratios for A) OS and B) PFS of patients diagnosed with NSCLC and exposed or not to antibiotics, according to the time window of antibiotic exposure.

ABX, Antibiotic; TW, Time Window; N/A, Not Available; HR, Hazard Ratio; CI, Confidence Interval ; NS, Non statistically Significant

CONCLUSION & PERSPECTIVES

The update of the meta-analysis confirms the previously reported deleterious effect of ABX on ICI treatment outcomes in NSCLC patients, taking into account the latest publications in the field. The impact of ABX exposure seems to be stronger when the exposition happens shortly before and after the initiation of the ICI treatment, whereas ABX use later during ICI treatment course does not seem to alter survival or to a lesser extent. The topic deserves further research to uncover if the effect will stand in other cancer types or with 1st line use of ICI together with chemotherapies and/or other approved combinations, elucidate the mechanisms at stake and improve the care of patients.

CONFLICT OF INTEREST

The study was sponsored by Da Volterra. AC, JC, CLB, RB and PAB are employees and JG and GZ are consultants for Da Volterra.

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