A Meta-Analysis of 23 Published Studies Demonstrates the Negative Impact of Antibiotics on the Efficacy of Immune Checkpoint Inhibitors in Non-Small-Cell Lung Cancer Patients

- The impact of antibiotics on the efficacy of immune checkpoint inhibitors (ICIs) was evaluated in 23 studies including 2,208 patients with non-small-cell lung cancer (NSCLC) for Progression Free Survival (PFS) and 5,560 patients for Overall Survival (OS).
- The median OS was reduced on average by 6.7 months (95% confidence interval [CI]: 5.1–8.4) in patients exposed to antibiotics.
- The pooled hazard ratio was 1.47 (95% CI: 1.13–1.90) for PFS and 1.69 (95% CI: 1.25–2.29) for OS revealing a significantly reduced survival in patients with NSCLC exposed to antibiotics.
- The magnitude of the effect depended on the time window of exposure to antibiotics with stronger deleterious effects reported when the patients took antibiotics around the initiation of cancer treatment.

Paris (France), 9th of April, 2020 – Da Volterra, a clinical-stage biopharmaceutical company developing innovative products to protect the intestinal microbiota from the damaging effects of antibiotics, today reports results from one of the first systematic reviews and meta-analyses on the impact of antibiotic use on immune checkpoint inhibitors’ efficacy in non-small-cell lung cancer patients. The study was published under the title “NSCLC Immunotherapy Efficacy and Antibiotic Use: A Systematic Review and Meta-Analysis” in the Journal of Thoracic Oncology (Impact Factor of 12.460 in 2018) and is available online at https://doi.org/10.1016/j.jtho.2020.03.002.

Da Volterra’s team conducted a systematic review of literature and performed a meta-analysis of the 23 most relevant studies: nine peer-reviewed publications, eight posters, and six conferences abstracts. Overall, 2,208 patients diagnosed with NSCLC were included in the meta-analysis for Progression Free Survival (PFS) and 5,560 patients in the meta-analysis for Overall Survival (OS).

The study showed that exposure to antibiotics around the initiation of ICIs treatment could reduce the median OS of patients by 6.7 months on average. The pooled hazard ratio was 1.47 (95% confidence interval [CI]: 1.13–1.90) for PFS and 1.69 (95% CI: 1.25–2.29) for OS. These results suggest that the use of antibiotics is correlated with a lower survival for NSCLC patients, which was hypothesized to be due to a decreased efficacy of ICIs when the gut microbiota is disrupted. The impact of antibiotics depended on the timeframe of their administration with respect to ICIs treatment initiation: the strongest effect was reported for limited time windows shortly before and after ICIs treatment initiation (from 60 days before to 60 days after treatment start).

“This study shows in a new light the importance of the state of the intestinal microbiota in cancer clinical outcomes; and it deserves to be recognized by hospital practitioners. It also highlights a need for large and well-conducted prospective studies further evaluating the correlation between cancer patients’ survival and changes of their intestinal microbiota.” said Dr. Renaud Buffet, MD, Medical Advisor for Da Volterra and co-author of the study.
When taken together with recent studies by Jin et al.¹ and Gopalakrishnan et al.² showing a correlation between a low-diversity microbiota and a reduced survival of cancer patients treated with ICIs, the meta-analysis further suggests that the intestinal microbiota may be a predictor and modulator of the response to ICIs. However, it is only with more robust clinical data that the medical community will be able to proffer the best recommendations regarding antibiotic use for cancer patients treated with ICIs.

“This meta-analysis clearly demonstrates that the use of antibiotics around the initiation of a treatment with immune checkpoint inhibitors should be considered with caution as it may negatively impact cancer patients’ survival. These results are an additional incentive to support the use of microbiota protective therapies such as DAV132 in association with immuno-oncology drugs.” declared Pierre-Alain Bandinelli, Chief Operating Officer at Da Volterra and co-author of the study.

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About DAV132:

DAV132 is a novel, patented colon-targeted adsorbent developed to protect the intestinal microbiota from the damaging effects of antibiotics. Co-administered with antibiotics, DAV132 has demonstrated its ability to selectively and safely suppress antibiotic disruption of the intestinal microbiota in multiple clinical trials. In patients taking antibiotics, DAV132 is developed for the prevention of *Clostridioides difficile* infections, as well as for the prevention of intestinal colonization by multi-drug resistant organisms and their dissemination. It is also anticipated to provide a significant clinical benefit, in combination with antibiotics, in patients undergoing allogeneic hematopoietic stem-cell transplantation (HSCT) as well as cancer patients treated with immune checkpoint inhibitors. DAV132 aims at being the first product protecting against the clinical consequences of intestinal microbiota dysbiosis to be available for physicians and patients.

About Da Volterra:

Headquartered in Paris (France), Da Volterra is a clinical-stage biopharmaceutical company whose vision is to be a trusted and acknowledged leader in the microbiota field. Da Volterra develops novel strategies aimed at protecting the intestinal microbiota to address large unmet medical needs in the infectious disease, gastroenterology, oncology, and hemato-oncology spaces. [https://davolterra.com](https://davolterra.com)

Contact:

Florence Séjourné, Chief Executive Officer of Da Volterra
+33 1 58 39 32 20 - press@davolterra.com

¹ [https://www.jto.org/article/S1556-0864(19)30286-2/abstract](https://www.jto.org/article/S1556-0864(19)30286-2/abstract)
² [https://science.sciencemag.org/content/359/6371/97](https://science.sciencemag.org/content/359/6371/97)