LECTURE SERIES 2024
CANCER RESEARCH

LUXEMBOURG INSTITUTE OF HEALTH | UNIVERSITÉ DU LUXEMBOURG

25 APR 2024
Thursday

LECTURE*
11.00am - 12.00pm

MEET & EAT*
Light lunch provided
12.30pm - 1.30pm

Oncolytic immunotherapy against human glioblastoma

ABSTRACT

A “first-in-human” phase 1 trial of intralesional injection of CAN-3110, an immunotherapeutic oncolytic based on herpes simplex virus 1 (HSV1), was conducted in 41 subjects with recurrent high-grade glioma (rHGG). The impact of CAN-3110 on the tumor immune microenvironment was assessed using immunohistochemistry, multiplexed immunofluorescence, TCR-beta DNA sequencing, and bulk RNA sequencing of paired pre- and post-treatment samples. These analyses were combined with patient features to identify potential biomarkers of therapy response in rHGG.

In IDH wild type recurrent glioblastoma (IDHwt rGBM) patients, post-treatment survival times were positively associated with positive pre-treatment HSV1 serology after controlling for additional covariates such as tumor volume, age, gender, CAN-3110 dose, etc. (HR = 0.16, $p < 0.001$, n = 32, CoxPH). Positive HSV1 serology was also significantly associated with clearance of CAN-3110 from injected tumors. Interestingly, increased intratumoral CD8 and CD4 T cell numbers following treatment were positively associated with prolonged survival in HSV1 seropositive patients ($p = 0.017$ and 0.026, respectively), but not when analyses were conducted including HSV1 seronegative patients. Likewise, post-treatment immune expression signatures (such as for antitumor cytokines, T cell traffic, etc.) were more strongly associated with prolonged survival for HSV1 seropositive patients than for seronegative patients, and most assessed immune signatures only became associated with survival after CAN-3110 treatment. Extended survival was also associated with increased TCR-beta diversity following therapy in both the tumor and in PBMCs.

Combined with a lack of observed dose-limiting toxicities and a median post-treatment survival of 14.2 months (95% CI: 9.5-15.7) in IDHwt rGBM patients with positive HSV1 serology, these data provide evidence that intralesional CAN-3110 treatment is capable of generating immune activation in a traditionally immunologically cold tumor in a way that influences survival time—particularly when patients have had prior exposure to HSV1. (clinicaltrials.gov NCT03152318)

SPEAKER

Prof. E. Antonio Chiocca, MD, PhD

Professor of Neurosurgery, Harvard Medical School
Brigham and Women’s Hospital, Neuroscience Center
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HOST:

Department of Cancer Research (LIH)
University of Luxembourg (UL)

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***Please note that registration is mandatory by sending an email to siu-thinh.ho@lih.lu**

Locations:

Lecture
CHL - Centre
*Room: **Amphitheatre***
4, rue Ernest Barblé
L-1210 Luxembourg

Meet & eat
LIH - DoCR (BAM)
*Room: **Mc Clintock***
6A, rue Nicolas-Ernest Barblé,
L-1210 Luxembourg

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