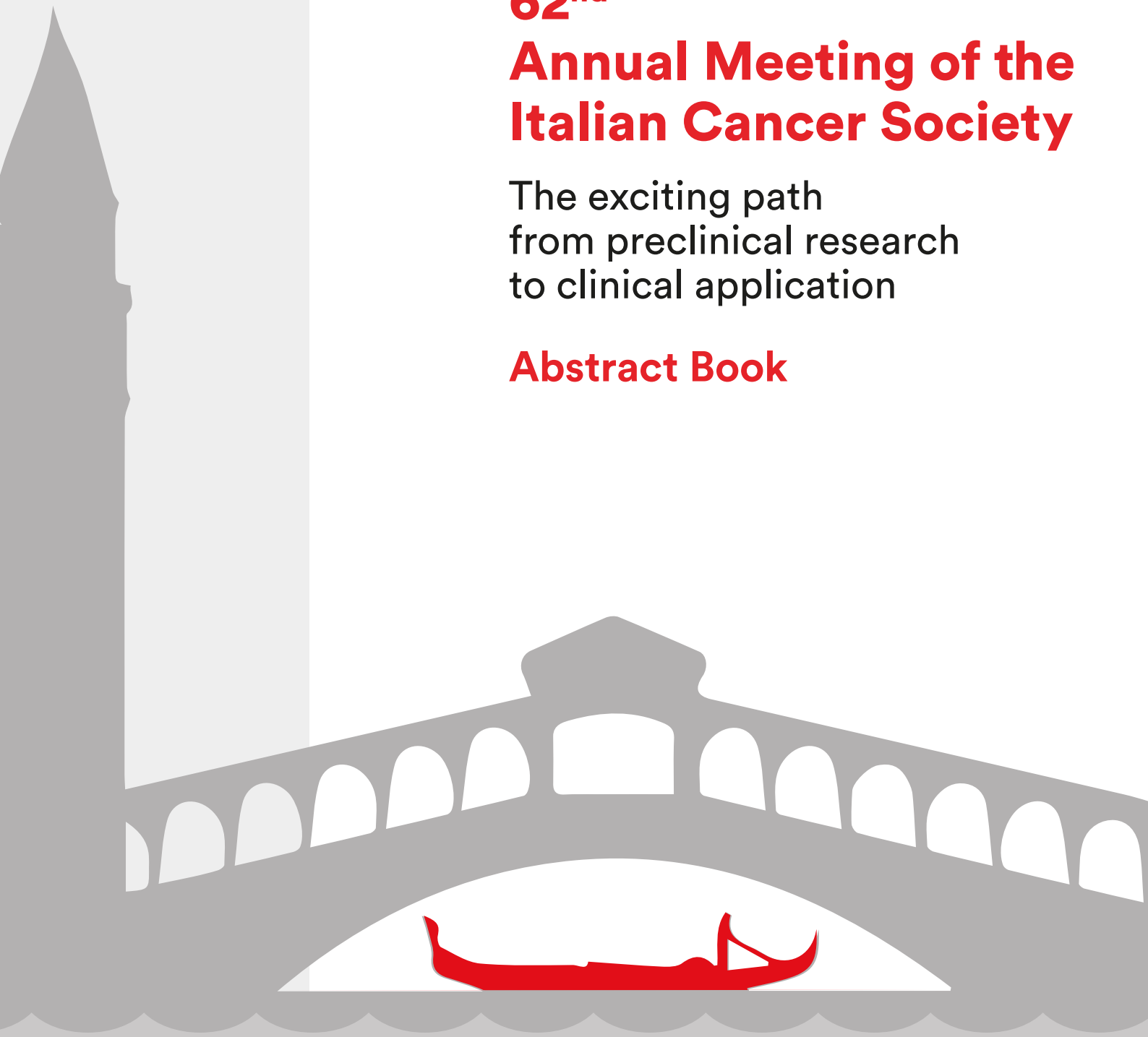
SIC

62nd Annual Meeting of the Italian Cancer Society

The exciting path
from preclinical research
to clinical application

Abstract Book



Venice, November 16-18, 2022

B18

Longitudinal liquid biopsy anticipates the risk for early death or hyper-progression in advanced Non-small cell lung cancer treated with immune checkpoint inhibitors

Zulato E. [1], Del Bianco P. [2], Nardo G. [1], Attili I. [3], Pavan A. [3], Boscolo Bragadin A. [4], Marra L. [4], Pasello G. [3], Fassan M. [5], Calabrese F. [5], Guarneri V. [3], Conte P.F. [3], Bonanno L. [6], Indraccolo S. [3]
(1) Basic and Translational Oncology Unit, Istituto Oncologico Veneto IOV IRCCS, Padova, Italy - Italy, (2) Clinical Research Unit, Istituto Oncologico Veneto IOV IRCCS, Padova, Italy - Italy, (3) Department of Surgery, Oncology and Gastroeneterology, Università degli Studi di Padova, Padova, Italy - Italy, (4) Immunology and Molecular Oncology Diagnostics Unit, Istituto Oncologico Veneto IOV IRCCS, Padova, Italy - Italy, (5) Surgical Pathology Unit, Department of Medicine, Università degli Studi di Padova, Padova, Italy - Italy, (6) Medical Oncology 2, Istituto Oncologico Veneto IOV IRCSS, Padova, Italy – Italy

Background: The introduction in clinical practice of immune checkpoints inhibitors (ICIs) have revolutionized treatment of advanced Non-small cell lung cancer (aNSCLC). However, a proportion of patients does not benefit from ICIs and could even derive detrimental effects. No predictive biomarkers are available for their early detection. Aims of our study was to characterize patients experiencing hyper-progression (HPD) and early death (ED) following ICIs by longitudinal liquid biopsy.
Methods: aNSCLC receiving ICIs were prospectively enrolled. Plasma was collected at baseline (T1) and after three/four weeks of treatment, according to treatment schedule (T2). Cell free DNA (cfDNA) was quantified and analyzed by NGS. cfDNA quantification and variant allele fraction (VAF) of tumor-associated genetic alterations were evaluated as static and dynamic parameters for their potential impact on outcome. The genetic alteration with the highest VAF (maxVAF) at baseline was considered as reference for NGS analysis.
Results: From March 2017 to August 2019, 171 patients were enrolled. Five cases matched criteria for HPD and 31 experienced ED; one overlapped. Median overall survival of HPD patients was 3.8 (95% CI: 1.7—N.A) versus 12.4 (95% CI: 9—13.7) months in control group (p=0.012).
Quantification of cfDNA at T2 and its absolute and relative variation (T2-T1) were significantly associated with the risk of ED (p=0.012, p=0.005, p=0.009). maxVAF relative change (T2-T1/T1) was significantly associated with the risk of experiencing HPD (p:0.02).
Discussion. Liquid biopsy performed early during treatment might anticipate detrimental effects of ICIs. Sequential assessment of cfDNA and maxVAF variation could permit to identify patients at higher risk of ED and HPD.

B19

The cellular and extracellular forms of the non-coding RNAs TERRA and TERC and TERT mRNA are dysregulated in human hepatocellular carcinoma

Grossi I. [1], Manganelli M. [1], Corsi J. [2], D'Agostino V.G. [2], Jurikova K. [2], Cusanelli E. [2], Molfino S. [3], Portolani N. [3], Salvi A. [1], De Petro G. [1]
(1) Department of Molecular and Translational Medicine, Division of Biology and Genetics, University of Brescia, Brescia - Italy, (2) Department of Cellular, Computational and Integrative Biology, CIBIO, University of Trento, Trento - Italy, (3) Department of Clinical and Experimental Sciences, Surgical Clinic, University of Brescia, Brescia - Italy

Telomeric repeat-containing RNA -TERRA- consists of different subtelomeric-derived transcripts (from 100 to 10 Kb in length) containing the canonical telomeric repeat sequence UUAGGG and sequences unique to the subtelomeric region of each chromosome. TERRA interacts with the telomerase core components (telomerase RNA component -TERC- and telomerase reverse transcriptase -TERT) and it is considered a regulator of telomere homeostasis by blocking the telomerase activity and altering the telomere length. Growing evidence indicates that TERRA is implicated in tumorigenesis, but little is known about its role in hepatocellular carcinoma (HCC). Here, we determined the expression levels of TERRA, TERC and TERT mRNA in tumor and peritumoral (PT) tissues as well as their circulating amount in the plasma of HCC patients. We quantified the levels of the same transcripts in the HCC cell lines and in their cognate extracellular vesicles (EVs) isolated from their secretome using the nickel-based isolation method. We used the HA22T/VGH and SKHep1C3 cells, sensitive and resistant to the anticancer drug sorafenib (a multi-kinase inhibitor). TERRA levels were obtained by qPCR as a mean of relative quantifications of TERRA from different telomeres (TERRA 1_2_10_13q, 15q, XpYp). ddPCR was used to detect TERC levels in plasma from HCC patients.
TERRA, TERC and TERT mRNA resulted dysregulated in HCC; in details TERRA was significantly down-regulated and TERC and TERT mRNA were up-regulated in HCCs versus PTs. For TERRA and TERT mRNA, the receiver operating characteristic (ROC) curve analyses indicated a significant ability in discriminating HCC from PT tissues. The circulating levels of TERRA and TERC were increased in the plasma of HCC patients versus controls and ROC analyses disclosed significant results. The expression profiling of these transcripts in vitro showed the increase of TERRA, TERC and TERT mRNA in HCC cells after sorafenib treatment and the ability of HCC cells to encapsulate TERRA and TERC in EVs. Our results highlight the differential expression of TERRA and TERT mRNA in HCC and PT tissues and of TERRA and TERC in liquid biopsies of HCC patients respect to healthy individuals. This provides novel insights on the contribution of these transcripts as innovative non-invasive molecular indicators of HCC and the involvement of TERRA and TERC in EVs of HCC cells in response to sorafenib treatment and in the development of the resistance (2022 PMID:35682861).