Paper #69 3255439 MOLECULAR ANALYSIS OF ARCHIVAL INFLAMMATORY MYOFIBROBLASTIC TUMOR TISSUE SAMPLES FROM EORTC 90101 "CREATE" AND CORRELATION WITH RESPONSE TO CRIZOTINIB Che-Jui Lee¹ ; Patrick Schöffski² ; Elodie Modave³ ; Bram Boeckx³ ; Diether Lambrechts³ ; Jozef Suflarsky⁴ ; Hans Gelderblom⁵ ; Jean-Yves Blay⁶ ; Agnieszka Wozniak¹ ¹ Department of Oncology, KU Leuven, Leuven, Belgium; ² Department of General Medical Oncology and Department of Oncology, UZ Leuven and KU Leuven, Leuven, Belgium; ³ VIB Center for Cancer Biology and Department of Human Genetics, VIB and KU Leuven, Leuven, Belgium; ⁴ National Cancer Institute, Bratislava, Slovakia; ⁵ Department of Medical Oncology, Leiden University Medical Center, Leiden, Netherlands; ⁶ Department of Medical Oncology, Centre Léon Bérard/Université Claude Bernard Lyon Institute, Lyon, France

Objective: Approximately 50% of inflammatory myofibroblastic tumors (IMFT) harbor rearrangements of anaplastic lymphoma kinase (ALK), the most common driver in this rare tumor type. A number of other genetic alterations have been described in individual patients (Antonescu et al. *Am J Surg Pathol.* 2015(7):957-967). EORTC 90101 "CREATE" is the only prospective, disease-specific Phase 2 clinical trial performed in IMFT so far (Schöffski et al. *Lancet Respir Med.* 2018(6):431-41). High anti-tumor activity was seen with the ALK-inhibitor crizotinib in ALK-rearranged IMFTs, but the trial results suggested that other molecular events may correlate with sensitivity to this agent. We performed an in-depth molecular analysis of archival tumor material from patients included in CREATE with the aim to identify other genetic alterations. **Methods:** DNA was isolated from archival IMFT tissue (primary tumor, local relapse or metastatic lesion). Samples were sequenced using Illumina HiSeq 4000. Shallow sequencing and GISTIC (genomic identification of significant targets in cancer) were performed to identify regions of the genome that are significantly amplified or deleted. Whole-exome sequencing was performed to assess the mutational landscape. Mutations affecting Cancer Consensus Genes (CCGs) were analyzed further. Survival analysis with Kaplan-Meier estimates and comparison with log-rank test were used to assess the correlation between molecular findings and clinical outcome of patients. Statistical analysis was performed using GraphPad Prism v7 and p values 2 samples and were mainly related to DNA damage and repair mechanisms, Wnt and RB-p53 signaling, and RTK-RAS-PI3K. **Conclusion:** We identified multiple molecular alterations in archival tumor material from IMFT and provide further insight in the molecular profile of this ultra-rare malignancy, which may potentially lead to the identification of novel targets for treatment.