

## Regular and Young Investigator Award Abstracts

### Biomarkers, Immune Monitoring, and Novel Technologies

#### 1 DISSECTING $\beta$ -CATENIN ASSOCIATED INFLAMMATION IN PATIENTS WITH DESMOID FIBROMATOSIS TO IDENTIFY PROGNOSTIC BIOMARKERS

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**Background** Desmoid fibromatosis (DF) is a locally aggressive rare tumor with high recurrence rate after surgery and unpredictable clinical course. Standard of care for DF patients is active surveillance; however, 30% of patients will progress and need active treatments. Biomarkers discriminating aggressive forms of DF are not available and prediction of progressing patients remains challenging. DF harbors mutations in  $\beta$ -catenin and a transcriptional 'inflammatory phenotype'. Cancer-associated inflammation is fostered by systemic factors and detectable in circulating immune cells. Blood leukocytes thus represent a promising source of prognostic biomarkers for DF patients. In this study we investigate phenotypic and functional features of peripheral blood immune cells and molecular profile of DF biopsies to identify DF patients at risk of progression and guide tailored therapeutic approaches.

**Methods** This is a prospective observational study enrolling patients with primary sporadic desmoid fibromatosis under active surveillance (n=80). Tumor and blood samples collected at diagnosis and during active surveillance will be studied by 1. transcriptomic analysis of DF biopsies; 2. multiparametric flowcytometry and functional profiling of blood cells; 3. RNA profiling of whole blood; 4. evaluation of plasma levels of cyto/chemokine and ctDNA of  $\beta$ -catenin variants. Levels of blood analytes will be correlated with patients' clinical outcome and integrated with immunological parameters.

**Results** Peripheral blood immune profile of 42 cases and 17 healthy donors (HD) shows that DF patients display at baseline an altered myeloid profile compared to HD, which is maintained in a subset of patients during the first year of active surveillance. An increase in immunosuppressive activated granulocytes and granulocytic myeloid-derived suppressor cells, defined by differential co-expression of CD15, CD11b, CD16 and LOX1, is observed, concomitantly, with a boost of monocyte subsets, defined by co-expression of CD33, CD11b, CD14, CD16, HLA-DR and PDL1. Immunosuppressive low density granulocytes are increased in progressing patients compared to HD and regressors. Of note, a significant up-regulation of immunosuppressive PMN-MDSC (defined as CD15+LOX-1+) is observed in DF harboring T41A mutation, but not in S45 mutated DF. Transcriptomic data of DF biopsies and of plasma analytes are ongoing.

**Conclusions** Systemic alterations of immunosuppressive and inflammatory myeloid cell subsets in peripheral blood of DF patients indicate that the inflammatory status detected at tumor site is reflected at systemic level. The altered myeloid profile supports the involvement of the immune system in DF onset and may represent a marker of disease aggressiveness.

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Trial Registration Not applicable.

#### REFERENCES

Not applicable.

**Ethics Approval** The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Fondazione IRCCS Istituto Nazionale dei Tumori di Milano (protocol code INT85/10).

**Consent** Written informed consent was obtained from the patient for publication of this abstract. A copy of the written consent is available for review by the Editor of this journal.

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