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Background

- Soft-tissue sarcomas (STS) are a group of rare, life-threatening, malignant tumors for which more efficient therapeutic options are necessary.
- Cancer immunotherapy has emerged as an active therapeutic option for several types of solid cancers.
- IMMUNOSARC was a European, single arm, non-randomized, open label, prospective phase Ib/II trial testing the double inhibition of angiogenesis (sunitinib) and PD-1/PD-L1 axis (nivolumab) in bone and STS.
- Since angiogenesis promotes immunosuppression, the combination therapy seeks to convert a cold into an inflamed microenvironment.
- The trial met its primary endpoint for STS, with 48% of patients free of progression at 6 months (m).¹
- Part of the results from the correlative studies are herein presented.

Methods

- Sixty-eight adult patients with selected subtypes of sarcoma have been enrolled during three years.
- Paraffin tumor blocks were prospectively collected at baseline (before Sunitinib initiation).
- Direct transcriptomics was performed using HTG Molecular Oncology Biomarker panel (HTG Molecular Diagnostics, Inc.; Tucson, AZ, USA).
- Differential gene expression was analyzed according to 6-m progression-free survival (PFS). A negative binomial generalized linear model was applied, using edgeR R/Bioconductor package. Functional enrichment analysis was performed using enrichR package and Gene Ontology (GO) database.

Table 1. First ten differentially expressed genes taking into account 6-m PFS rate.

	logFC	PValue
<i>DLGAP5</i>	1,09729	0,00002
<i>AURKB</i>	0,97972	0,00002
<i>NR4A3</i>	-1,93734	0,00003
<i>MAOB</i>	-2,20566	0,00003
<i>WHSC1</i>	0,87751	0,00008
<i>NUF2</i>	0,93483	0,00010
<i>ABHD2</i>	-1,62988	0,00011
<i>CDC20</i>	1,33925	0,00013
<i>ECT2</i>	1,12292	0,00013
<i>NUSAP1</i>	1,10916	0,00015

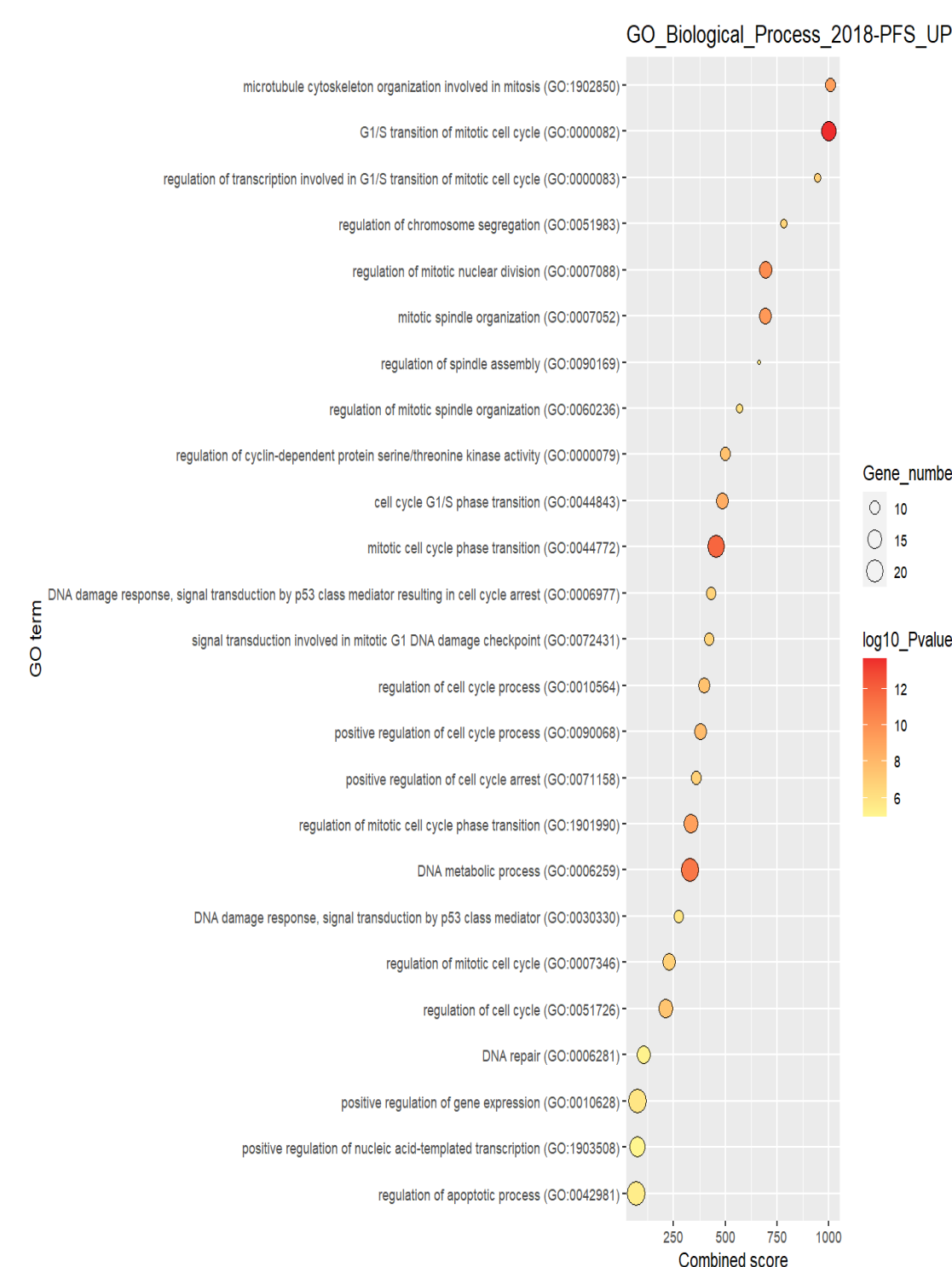


Figure 1. GO analysis showing Biological Processes associated to selected up-regulated genes taking into account 6-m PFS rate.



Figure 2. GO analysis showing Biological Processes associated to selected down-regulated genes taking into account 6-m PFS rate.

Table 2. First ten differentially expressed genes taking into account Overall Survival (OS).

	logFC	PValue
<i>PLA2G2A</i>	3,48814	0,00001
<i>ALDH1A1</i>	-2,41818	0,00004
<i>ITGA8</i>	-1,75482	0,00008
<i>TICAM1</i>	0,74314	0,00028
<i>NR4A3</i>	-1,67382	0,00033
<i>FAM105A</i>	-1,00283	0,00034
<i>S100B</i>	2,46255	0,00036
<i>PDGFB</i>	-0,84179	0,00037
<i>PDGFD</i>	-1,48592	0,00038
<i>CHAD</i>	-2,86794	0,00047

Results



Figure 3. GO analysis showing Biological Processes associated to selected up-regulated genes taking into account OS.



Figure 4. GO analysis showing Biological Processes associated to selected down-regulated genes taking into account OS.

Conclusions

- DNA damage repair (DDR) and cell cycle-related processes seemed to be associated with worse outcome to immunotherapy-based schemes.
- Further studies are warranted to understand the potential added value of cell cycle inhibitors or DDR-targeted therapies to immunotherapy.

Acknowledgments

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Disclosures

SL has nothing to disclose.

References

1.Martin-Broto J, Hindi N, Grignani G, et al. Nivolumab and sunitinib combination in advanced soft tissue sarcomas: a multicenter, single-arm, phase Ib/II trial. J Immunother Cancer. 2020 Nov;8(2):e001561.

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