MMT while 76 received nMMT. Patients receiving MMT displayed higher overall response rate (37.3% vs 12.9%), median progression-free-survival (PFS 5.8 months, 95% CI 4.1—7.5 vs 3.6 months, 95% CI 2.5—4.8, p=0.041; HR 0.679, 95% CI 0.467—0.987) and median overall-survival (mOS 35.1 months, 95% CI not evaluable vs 8.5 months, 95% CI 3.8 — 13.2; HR 0.431, 95% CI 0.250 — 0.744, p=0.002). Superiority in OS and PFS persisted in multivariable models. Among 61 pretreated patients receiving MMT, 37.5% had superior PFS compared to the prior line (PFS2/PFS1 ratio $\geq$ 1.3). Higher OS (p=0.001) and PFS (p=0.049) were observed for patients with higher actionability evidence (ESCAT tier I) alterations, while no difference was observed in lower evidence levels.

Table: 71P Most frequent actionable genes

Alteration	Total number	Treated patients	Drug administered	ESCAT at discussion	ORR
PIK3CA	51	4	Alpelisib	IA	1/4 (25%)
BRCA2	32	19	PARP-i	IA	7/19 (37%)
BRAF V600	20	2	BRAF + MEK-i	IIIA	1/2 (50%)
ERBB2	17	1	Trastuzumab + pertuzumab	IIIA	1/1 (100%)
TMB-HIGH	16	4	Anti-PD(L)-1	IC	2/4 (50%)
ATM	15	2	PARP-i	X	0/2 (0%)
MSI-HIGH	14	8	Anti-PD(L)-1	IC	4/8 (50%)
BRCA1	11	9	PARP-i	IA	2/9 (22%)
RET	10	10	RET-i	IIIA	7/10 (70%)

Conclusions: We report real-world data of the first Italian experience of MTB application in clinical practice. Our work shows that MTBs can yield valuable clinical benefit in terms of OS and PFS. Biomarkers with lower actionability ESCAT level appear to be linked to lower clinical benefit.

Clinical trial identification: This study is approved by IEO Ethical Committee with the reference number UID 3572.

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72P MDM alterations in patients with advanced or metastatic cancers

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Background: Oncogenic alterations in MDM represent important therapeutic targets in various type of cancer. We aimed to assess the prevalence of its incidence together with p53 status in advanced solid tumors based on commercially available NGS panel and to monitor patients' clinical pathway care.

Methods: Between 2019-2022, 740 patients were included for molecular testing in the Center of Excellence for Precision Oncology, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland. The population with MDM alterations was extracted for this analysis. We analyzed their therapeutic options over the years, access to clinical trials and impact on patients' survival.

Results: In our cohort, 48 patients (6.5%) had been identified with MDM alterations as amplification (38), rearrangements (5), and SNPs (5). The most common histology were sarcomas (22), cholangiocarcinoma (3), gastric cancer (3), colorectal cancer (3), breast cancer (3), ovarian cancer (2), salivary gland cancer (2), melanoma (2), urothelial cell carcinoma (2), other (6). In sarcoma, 20/22 had amplification of MDM2, 6/22 rearrangements (MDM2-PPFIA2 rearrangement, MDM2-CSMD1 rearrangement, MDM2-EYS rearrangement) and SNPs (I388V and R332P). The predominant histology types were liposarcomas 14 (64%), sporadically MDM changes were found in rhabdomyosarcoma, osteosarcoma, angiosarcoma, leiomyosarcoma, undifferentiated spindle cell sarcoma and malignant peripheral nerve sheath tumour.

Conclusions: The detection of MDM alterations allows for access to targeted therapies, especially in sarcomas, which may be an important therapeutic option in these rare cancers.

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73P Automated detection of typical and atypical mitotic figures for improving survival prediction in breast cancer

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Background: The number of typical and atypical (defined as mitoses with any morphological appearance other than the typical forms) mitotic figures (MFs) and a high atypical-to-typical mitosis ratio are strongly associated with tumour aggressivity, survival rates, and a predictor of poor response to chemotherapy in breast cancer. Manual detection is time consuming, especially on whole slide images (WSIs). An automated approach is therefore necessary to investigate these aspects on a larger scale. We demonstrate that deep learning can be used to automate this detection, improving on the performance of pathologists.

Methods: All MFs in the mammary carcinoma dataset (21 hematoxylin and eosin (H&E)-stained WSIs with ~14 000 MFs and ~36 000 hard negatives) were labelled as typical or atypical. These slides (originally scanned on a Leica scanner) were then rescanned on six other scanners (2x Hammamatsu, 2x 3DHISTECH, Philips, Olympus), and the annotations were registered. This gave a large, multi-scanner dataset, which was used to train a YOLOv6 deep learning object detection model. For testing, all MFs in the (human) TUPAC16 and MIDOG21 datasets were labelled by two pathologists as either typical or atypical. In cases of disagreement, a third reader gave a consensus. We used the alternative version of the TUPAC16 dataset provided by the same authors as the MIDOG21 dataset to reduce potential label bias. We then ran our model on these images and compared the mean average precision (mAP) vs the consensus to the mAPs of the two individual pathologists vs the consensus.

Results: The mAP of our model (0.80) was higher than the average mAP of the two pathologists (0.75, $p<0.05$), showing that the model can successfully automate the process of MF detection. There was considerable disagreement in the labelling by the two pathologists (14% of cases). By automating the process we reduce this variability, meaning we can more consistently predict clinical outcomes (e.g. survival rates) from our results.

Conclusions: The numbers of both typical and atypical MFs are indicators of patient survival and response to treatment. We have demonstrated an automated deep learning model that can accurately detect these figures and could thus be used for patient survival prediction.

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