(67.6%), respectively. Seventeen patients (23.0%) had access to either genotype-matched therapy, off-label drugs or were enrolled in clinical trials.

Conclusions: The detection rate of actionable and druggable genomic alterations and the proportion of patients who proceeded to another therapy based on the CGP testing after completion of standard treatments were higher than previously reported for other solid tumors. Therefore, CGP tests may be beneficial in daily practice for the treatment of malignant melanoma patients.

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A-399

The RoMEO study: a real-world, observational, prospective investigation of dabrafenib and trametinib combination treatment in patients with BRAF V600 unresectable or metastatic cutaneous melanoma

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Background: Cutaneous melanoma is the most aggressive form of skin cancer, although outcomes have improved markedly with targeted therapies and immune checkpoint inhibitors. The combination of the BRAF inhibitor dabrafenib and the MEK inhibitor trametinib (D + T) administered as first or second-line therapies for locally advanced or metastatic melanoma with BRAF V600 mutation has improved progression free survival (PFS) and overall survival (OS) in randomized trials [1]. The aim of this study, conducted under the auspices of the French National Skin Cancer Task Force, was to further investigate the efficacy and clinical use of D + T in a real-world setting in France.

Methods: We assessed the real-world efficacy of first or second-line D + T at 12 months in 240 patients with BRAF V600 unresectable or distant metastatic cutaneous melanoma from 38 centers. Patient data were collected at baseline and at 3, 6 and 12 months. PFS and OS were computed in the study overall and by treatment line.

Results: Among an assessable population of 224 patients, 101 (45.1%) presented with 3 or more metastatic sites and 75 (33.5%) with a brain metastasis. In addition, 33 (19.1%) had lactate dehydrogenase above twice the upper limit of normal (2xULN). In total, 165 and 59 patients received D + T as first and second-line therapies respectively. PFS rates at 12 months were 29.9% overall (95% CI: 23.8-36.2) and 29.8% (95% CI: 22.7-37.2) and 30.4% (95% CI: 19.1-42.6) for first and second-line treatment groups respectively. The OS rate at 12 months among all patients was 54.8% (95% CI: 47.6-61.3). Of the safety population (n = 235), 139 (59.1%) and 40 (17.0%) reported a treatment-related adverse event or serious adverse event respectively. No new safety signals were observed.

Conclusions: Clinical outcomes after treatment of the study population with D + T in France were similar whether deployed as a first or second-line treatment. RoMEO complements the findings from COMBI-d and COMBI-v and provides additional data on patients excluded from these pivotal trials due to brain metastases or following other treatments. Further work is underway to characterize and assess tumor kinetics as a potential predictor of D + T treatment response.

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Merkel cell carcinoma

A-394

All-trans retinoic acid activity in Merkel cell carcinoma cells: implication of the retinoid pathway

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Background: Merkel cell carcinoma (MCC) is a rare but aggressive skin cancer. About 80% of MCCs, are linked to oncogenic Merkel cell polyomavirus (MCPyV). The currently available MCC therapeutic options are unsatisfactory, therefore novel therapeutic approaches are required. The biological activity of all-trans retinoic acid (ATRA) is mediated by RAR/RXR receptors that activate genes crucial for cell differentiation. Dysregulations of RAR/RXR receptors lead to carcinogenesis. ATRA displays a strong in vitro/in vivo antitumor activity in different carcinoma types, but its effect in MCC is currently unknown. Herein, we investigated cell death effects of ATRA in MCC cells.

Methods: For this purpose, in vitro in MCPyV-positive (MCCP), i.e., PeTa and WaGa, and -negative (MCCN), i.e., MCC13 and MCC26, MCC cell lines and control, normal human lung fibroblasts MRC-5 were tested with ATRA. The effect of ATRA was evaluated by testing MCC cell proliferation, migration and colony formation abilities. Apoptosis/cell death were evaluated via Annexin-V/P.I. assays. Apoptosis was evaluated by RT^2 Profiler PCR mRNA array and by western blot (WB) analysis. Retinoid pathway was evaluated by RT^2 Profiler PCR mRNA array.

Results: ATRA treatment led to a significant reduction in MCC cell proliferation, migration and clonogenicity, while increasing apoptosis/cell death in MCC cell lines compared to untreated cells. MCCP cells were slightly more ATRA-sensitive compared to MCCN cells. No significant effects have been found in the ATRA-treated control cell line. Gene expression array indicated a significant overexpression of several pro-apoptotic genes in MCC cells. Consistently, high levels of pro-apoptotic proteins have been found following ATRA treatments in MCC cells, while being almost undetectable in untreated cells. Pro-apoptotic markers were almost undetectable in ATRA-treated MRC-5. Numerous retinoic signaling genes were differentially expressed in ATRA-treated MCC cells compared to untreated cells.

Conclusions: Overall, in vitro data indicate that ATRA is effective in reducing MCC cell growth, while presenting strong pro-apoptotic effects and favoring cell death, by modulating the retinoic receptor pathway. These results, for the first time, point to ATRA as a potential novel effective antineoplastic drug for the MCC therapy.

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