TEMOZOLOMIDE IN MGMT UNMETHYLATED GLIOBLASTOMA
DRUG CHLORPROMAZINE AND ITS COMBINATION WITH MAPKi, in patients with BRAF-altered pLGG regardless of prior MAPKi

CLUSIONS: Tovorafenib provided clinically meaningful tumor responses, and maculopapular rash (38%). Tovorafenib dose modifications occurred in 50% of pts.

April 2020 to October 2022, 69 (RANO-HGG) and 76 (RANO-LGG) of 77 patients in arm 1 were evaluable at exploratory endpoints. RESULTS: As of December 22, 2022, 69 (RANO-

3.5 weeks on/1 week off. Brain MRI was performed within 14 days before Stage 1. Day One Biopharmaceuticals, Brisbane, CA, USA, St. Louis Children's Hospital (NCH), St. Louis, MO, USA,

The ORR in patients previously treated with MAPKi (n = 41 [RANO-HGG] and 45% [7 PRs; 7 MRs] (RANO-LGG). Among 136 patients in arms 1 and 2 of FIREFLY-1, the most common treatment-related adverse events included grade 1-2 anorexia (26%), fatigue (22%), nausea (23%), vomiting (14%), alopecia (30%), and maculopapular rash (38%). Tovorafenib dose modifications occurred in 50% of pts.

October 2022, 192 recurrent GBM pts were enrolled from 29 Cancer Centres in Italy: median age 61 years, 29% of pts had K670E BRAF, 5% BRAF V600E. All pts had relapse after Stupp treatment, good performance status (ECOG PS 0-1), and no prior treatment with BRAF or MEK inhibitors. targ. enrollment in first 15 pts, and phase 2 if at least one 90% and ORR >= 50% in at least one of the 4 regions (North, South, West, East) of Italy. RESULTS: as of December 22, 2022, 69 (RANO-

between arms. CONCLUSIONS: To investigate the safety and clinical activity of REG in recurrent GBM. Eligibility criteria included: age >= 18 years, ECOG PS 0-1, recurrent GBM after Stupp therapy, good performance status, and no prior regimens for recurrent GBM. REG was administered orally at 400 mg daily on a 3-week schedule, and then weekly every 3 weeks for a total of 2 cycles. RESULTS: as of December 22, 2022, 69 (RANO-HGG) and 76 (RANO-LGG) of 77 patients in arm 1 were evaluable at exploratory endpoints. RESULTS: as of December 22, 2022, 69 (RANO-

regression analysis, the ORR in patients previously treated with MAPKi (n = 41 [RANO-HGG]) was 29% (7 PRs; 7 MRs; 22% SD; 33% PD). Median OS for the whole population was 14.7 months, with a median follow-up of 16.5 months. RESULTS: as of December 22, 2022, 69 (RANO-HGG) and 76 (RANO-LGG) of 77 patients in arm 1 were evaluable at exploratory endpoints. RESULTS: as of December 22, 2022, 69 (RANO-

The use of REGOMA in recurrent GBM is supported by a good toxicity profile of REG in recurrent GBM pts. CONCLUSIONS: REGOMA-OS showed promising activity in recurrent glioblastoma (GBM) patients with unmethylated MGMT. Drug repurposing can represent a safe and inexpensive way to bring novel pharmacological approaches from bench to bedside.
H3 K27M-mutant glioma were first described as a new grade IV entity in the 2016 WHO classification. Current studies have focused on its common pediatric appearance, increasing the need to better understand this entity in adults. Here we report a multicentric, retrospective analysis of 70 diffuse midline glioma in adults. We included molecularly confirmed H3K27M-mutant glioma in patients >18 years of age between 2015-2022. Clinical, radiological, and surgical features were analyzed. Univariate and multivariate analyses were then performed to identify prognostic factors. The study was approved by the ethics committee (PV4904). Overall, 70 patients were identified, with a mean age of 36.13 years at the initial diagnosis. Median overall survival was 13.62 ± 14 months. H3K27M-mutated glioma showed a midline involvement in 61.4%. Clinically, obstructive hydrocephalus was observed in almost half of the patients (46.3%). Gross total resection (GTR) was achieved in 14.3% of all patients. 30.4% had a subtotal resection (STR), and 55.1% received a biopsy. Intraoperative cryosection resulted in low-grade glioma in 23%, high-grade glioma in 63.9% and no tumor in 11.1%. Tumors located in telencephalon/diencephalon/myelencephalon were associated with a poorer OS, while a location site in the mesencephalon/metencephalon showed a significantly longer survival (8.3 vs. 16.2 months, p = 0.009). Preoperative Karnofsky Performance Score (KPS) below 80 showed a reduced OS (6 vs. 11.24 months, p = 0.03). Patients, who received resection (GTR/STR) showed no significant survival benefit compared with biopsied patients (9.6 vs. 8 months, p = 0.4817). The present study describes surgical features of DMG with H3K27M mutation in one of the most extensive multicentric studies to date in adult patients. Our data show that location and preoperative KPS impact OS significantly in DMG. Furthermore, in our dataset resection of K27M-mutated glioma provided no significant survival benefit compared with biopsy.