CATNON trial

- Epigenetic landscape reorganisation and reactivation of embryonic development genes are associated with malignancy in IDH-mutant astrocytoma
- Epigenetic landscape reorganization and reactivation of embryonic development genes are associated with malignancy in IDH-mutant astrocytoma
- MGMT promoter methylation in 1p19q-intact gliomas
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- Mitotic count is prognostic in IDH mutant astrocytoma without homozygous deletion of CDKN2A/B. Results of consensus panel review of EORTC trial 26053 (CATNON) and EORTC trial 22033-26033
- Current Considerations in the Treatment of Grade 3 Gliomas
- Temozolomide and Radiotherapy versus Radiotherapy Alone in Patients with Glioblastoma, IDH-wildtype: Post Hoc Analysis of the EORTC Randomized Phase III CATNON Trial
- Treatment of anaplastic gliomas: evidences and controversies

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●EORTC 26053 (CATNON trial) – Direct support for RT plus temozolomide in patients with IDH-mutant grade 3 astrocytoma is based on results of the EORTC 26053 CATNON trial. In CATNON, 751 patients with newly diagnosed 1p/19q-non-codeleted anaplastic (grade 3) gliomas (both IDH-mutant and IDH-wildtype) were randomly assigned to one of four treatment arms: RT alone, RT with concurrent daily temozolomide, RT with concurrent daily temozolomide plus up to 12 cycles of monthly adjuvant temozolomide, and RT plus up to 12 cycles of monthly adjuvant temozolomide

As of a second interim analysis with a median follow-up of 56 months, the use of adjuvant temozolomide improved median survival compared with no adjuvant temozolomide in the overall population (82 versus 47 months; HR 0.64, 95% CI 0.52-0.79) [33]. When analyzed according to IDH mutation status, however, the benefit of adjuvant temozolomide was observed only in IDH-mutant tumors (117 versus 78 months; HR 0.48, 95% CI 0.35-0.67) and not in IDH-wildtype tumors (21 versus 19 months; HR 1.0, 95% CI 0.75-1.33).

By contrast, concurrent temozolomide did not improve survival in the overall population (67 versus 60 months; HR 0.97, 99% CI 0.73-1.28), although a nonsignificant trend towards benefit in IDH-mutant tumors was present (117 versus 92 months; HR 0.80, 95% CI 0.58-1.10). Longer follow-up is needed to determine whether there is a clinically important benefit to concurrent temozolomide in patients with IDH-mutant tumors, but at present this is not observed in patients also receiving adjuvant temozolomide treatment.

Both pivotal trials of RT with or without PCV in newly diagnosed grade 3 oligodendroglioma/oligoastrocytoma (EORTC 26951 and RTOG 9402) included some patients with what would now be categorized as IDH-mutant grade 3 astrocytomas; in these trials, the benefit of PCV was most evident in histologic oligodendrogliomas, although there was a nonsignificant trend towards improved survival in the subgroup of IDH-mutant, non-codeleted tumors as well. This observation, along with the greater convenience and tolerability of temozolomide, has led most clinicians to adopt temozolomide as the standard adjuvant chemotherapy in grade 3 astrocytomas, rather than PCV. The role of PCV in oligodendroglial tumors is discussed in detail separately. (See “Treatment and prognosis of IDH-mutant, 1p/19q-codeleted oligodendrogliomas in adults”, section on 'Rationale for RT plus chemotherapy'.)

In contrast to the CATNON trial of RT plus temozolomide as well as trials of RT plus PCV in oligodendroglial tumors, trials of chemotherapy alone (PCV or temozolomide) have not shown an improvement in survival compared with RT alone in newly diagnosed grade 2 or grade 3 diffuse gliomas. Accordingly, the available data suggest that chemotherapy alone is inferior to RT plus chemotherapy in newly diagnosed patients [1)]

Anaplastic astrocytoma without 1p/19q co-deletion is a rare primary central nervous system tumor occurring primarily in middle-aged adults and associated with a median survival of 5-10 years. The major corner stone of treatment is maximal safe neurosurgical resection, followed by radiotherapy and chemotherapy. Several clinical trials addressed the optimal adjuvant treatment; however, interpretation has been challenged by the recent molecular marker-based reclassification of tumour. The interim study of the CATNON trial strongly suggests the addition of 12 adjuvant cycles of temozolomide in addition to radiotherapy after maximal safe resection in patients with anaplastic astrocytoma without 1p/19q codeletion. Based on more recently presented data from the second interim analysis of the CATNON trial and from the molecular analysis, benefit from temozolomide during and after radiotherapy is limited to patients with isocitrate dehydrogenase-mutated anaplastic astrocytoma. Given the small patient number in the single subgroups and the so far missing neurocognitive and quality of life data, more mature analyses needs to be awaited to draw final conclusions on the application of concurrent temozolomide treatment for the daily routine in patients who already are scheduled for adjuvant temozolomide. Further molecular analysis is ongoing to define personalised treatment approaches in patients with anaplastic astrocytoma [2)].

Treatment of noncodeleted AA based on preliminary results from the CATNON clinical trial consists of maximal safe resection followed by radiotherapy with post-radiotherapy temozolomide (TMZ) chemotherapy. The role of concurrent TMZ and whether IDH1 subgroups benefit from TMZ is currently being evaluated in the recently completed randomized, prospective Phase III clinical trial, CATNON [3)].

In 2017 the Interim results from the CATNON trial was that adjuvant temozolomide chemotherapy was associated with a significant survival benefit in patients with newly diagnosed non-co-deleted anaplastic glioma. Further analysis of the role of concurrent temozolomide treatment and molecular factors is needed [4)].

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