Clinical Trial Lancet Oncol. 2026 Jan;27(1):45-56. doi: 10.1016/S1470-2045(25)00614-X.

Concurrent and adjuvant temozolomide for 1p/19q non-co-deleted anaplastic glioma (CATNON; EORTC study 26053-22054): final and exploratory analyses of a randomised, open-label, phase 3 trial

Martin J van den Bent [1], Santoesha A Ghisai [2], Wolfgang Wick [3], Marc Sanson [4], Alba Ariela Brandes [5], Paul M Clement [6], Sara C Erridge [7], Michael A Vogelbaum [8], Anna K Nowak [9], Jean-François Baurain [10], Warren P Mason [11], Helen Wheeler [12], Emeline Tabouret [13], Sanjeev Gill [14], Matthew Griffin [15], Walter Taal [2], Roberta Rudà [16], Michael Weller [17], Catherine McBain [18], Jaap C Reijneveld [19], Roelien H Enting [20], Sébastien Tran [21], Thierry Lesimple [22], Martin Kocher [23], Anja Gijtenbeek [24], Elizabeth Lim [25], Ulrich Herrlinger [26], Peter Hau [27], Frederic Dhermain [28], Kenneth Aldape [29], Robert B Jenkins [30], Hendrikus Jan Dubbink [31], Johan M Kros [31], Pieter Wesseling [32], Youri Hoogstrate [2], Sarah Nuyens [33], Vassilis Golfinopoulos [33], C Mircea S Tesileanu [34], Thierry Gorlia [33], Pim French [2], Brigitta G Baumert [35]

PMID: 41449147 DOI: 10.1016/S1470-2045(25)00614-X

Abstract

Background: The CATNON trial investigated the benefit of the addition of concurrent or adjuvant temozolomide to radiotherapy in individuals with anaplastic astrocytoma. We report the long-term follow-up of the study focusing on the individuals with isocitrate dehydrogenase (IDH) mutated (IDHmt) tumours.

Methods: This randomised, open-label, phase 3 study in 137 institutions across Australia, Europe, and North America included participants aged 18 years or older with newly diagnosed 1p/19q non-co-deleted anaplastic gliomas and a WHO performance status of 0-2. Participants were randomly assigned (1:1:1:1) centrally using a minimisation technique to radiotherapy alone (59·4 Gy in 33 fractions), radiotherapy with concurrent oral temozolomide (75 mg/m^2 per day), radiotherapy with adjuvant oral temozolomide (12 4-week cycles of 150-200 mg/m^2 temozolomide given on days 1-5), or radiotherapy with both concurrent and adjuvant temozolomide. Participants were stratified by institution, WHO performance status score, age, 1p loss of heterozygosity, the presence of oligodendroglial elements on microscopy, and MGMT promoter methylation status. The primary endpoint was overall survival adjusted by stratification factors at randomisation in the intention-to-treat population. The eighth amendment of the study protocol (June 27, 2011) incorporated analysis of IDH mutational status into the study. We report the intention-to-treat analysis and the exploratory analysis within the population of participants with astrocytoma with an IDH mutation. As the safety data have been published previously, no safety data are reported. This trial is registered with ClinicalTrials.gov, NCT00626990, and is completed.

Findings: Between Dec 4, 2007, and Sept 11, 2015, 1407 participants were registered and 751

participants were randomly allocated, 444 of whom were diagnosed with an IDHmt tumour. After a median follow-up for overall survival of 10·9 years (IQR 9·5-12·7), in the intention-to-treat population, adjuvant temozolomide improved overall survival compared with no adjuvant temozolomide (hazard ratio [HR] 0·65 [95% CI 0·54-0·77]), but concurrent did not compared with no concurrent temozolomide (HR 0·91 [0·76-1·08]). In univariable analysis of the participants with an IDHmt tumour, concurrent temozolomide had no statistically significant effect on overall survival (median 9·7 years [8·2-12·5] vs 7·2 years [6·2-9·4]; HR 0·81 [0·63-1·04]), but median overall survival was 12·5 years (95% CI 9·4-15·0) with adjuvant temozolomide compared with 6·0 years (5·1-7·2) with no adjuvant temozolomide (HR 0·54 [0·42-0·69]). No benefit of temozolomide, neither concurrent nor adjuvant, was observed in participants with IDH wild-type tumours. Methylation-based subtyping and several DNA alterations (eg, amplification of PDGFRA and CDK4, homozygous deletion of CDKN2A, and total copy number variation) were associated with worse outcome, none of which was predictive for benefit to temozolomide.

Interpretation: Long-term follow-up confirms that radiotherapy followed by 12 cycles of adjuvant temozolomide without concurrent temozolomide during radiotherapy improves survival for individuals with aggressive IDHmt astrocytoma.

Funding: MSD.