

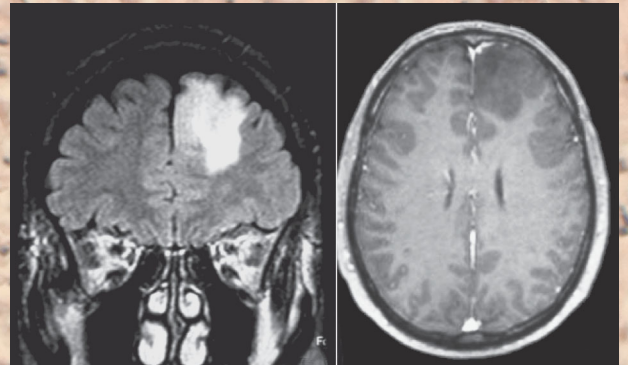
# European Association of NeuroOncology Magazine

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**Interview with Dr Martin van den  
Bent (Rotterdam) About the EORTC  
TAVAREC Trial on Recurrent Grade-II  
and -III Gliomas**

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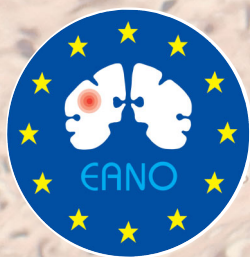
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# Interview with Dr Martin van den Bent (Rotterdam) About the EORTC TAVAREC Trial on Recurrent Grade-II and -III Gliomas

Ufuk Abacioglu

From the Department of Radiation Oncology, Neolife Medical Center, Istanbul, Turkey

**Q:** Dr van den Bent, what can you tell us about the ongoing TAVAREC trial on grade-II and -III gliomas? What is its background and objective?

**A:** The background of the trial are the reports on the activity of bevacizumab in recurrent glioblastoma and a few reports on bevacizumab in recurrent grade-III glioma. None of those trials were controlled and the reported activity in recurrent grade-III glioma was similar compared to glioblastoma trials. The obvious question is whether bevacizumab given to grade-III tumours treated at recurrence with temozolomide improves outcome. The principle investigators of this EORTC study are Ahmed Idbaih, a neurologist at the La Salpêtrière Institute in Paris and myself.

**Q:** How is the trial designed? Which patients are eligible for this trial?

**A:** The trial has been set up as a randomized phase-II trial investigating temozolomide as a single agent in the control arm, and the combination temozolomide/bevacizumab in the other arm. Because progression-free survival is less reliable in trials on anti-VEGF agents, overall survival at 12 months is the primary endpoint. To explore the clinical significance of any difference in PFS – should that be observed –, quality of life and cognitive functioning are also assessed. The hypothesis is that bevacizumab may help to maintain good quality of functioning, alternatively, the development of unenhancing gliomatosis cerebri as observed during treatment with anti-VEGF agents may induce deterioration even in the absence of progression as assessed on contrast-enhanced T1 MR images. Eligible for this study are patients with a recurrent and dedifferentiated grade-II or -III glioma, without combined 1p/19q loss, showing either measurable disease or having a confirmed (secondary) glioblastoma at surgery for the recurrence.

**Q:** What are the schemes and durations of treatment in both arms?

**A:** The patients of arm A (the control arm) are receiving temozolomide day 1–5 every 4 weeks for 12 months, in the

other arm (the investigational arm) they receive the same temozolomide regimen but in combination with iv bevacizumab 10 mg/kg every 2 weeks, with bevacizumab given until progression.

**Q:** What are the stratification factors?

**A:** The stratification factors are the treating institution, initial histology (grade II versus III), WHO PS: 0 + 1 versus 2, and prior treatment (RT alone, TMZ or PCV alone, vs TMZ/RT).

**Q:** Why did you choose overall survival at 1 year as the primary endpoint, while 6-month progression-free survival is preferred in most recurrent high-grade glioma trials?

**A:** Well, PFS 6 is actually only an established endpoint for trials on recurrent glioblastoma. But, more importantly, bevacizumab is likely to obscure the diagnosis of radiological progression by the normalization of the increased leakiness of tumour vessels that is inherent to anti-VEGF agents. Therefore, in general, neuro-oncology trials with bevacizumab in recurrent glioma should have OS as the primary endpoint.

**Q:** Do you have any planned translational studies for investigating the molecular subtypes?

**A:** We are in particular interested in IDH status and MGMT promoter status and we will assess markers of the VEGF pathway in tumour tissues.

**Q:** How is response assessed in this trial? Do you use the RANO criteria?

**A:** Indeed, we will be using the RANO criteria. One of the reasons to develop the RANO criteria were the issues observed in patients treated with bevacizumab: in particular the diagnosis of unenhancing progression and even the development of frank gliomatosis. Also, the RANO criteria allow to continue treatment in case of unclear progression, and call progression with hindsight if the further clinical developments show that progression was indeed present.

**Q:** *How is the accrual and when do you expect to reach the accrual goal? When can we get the first results?*

**A:** Accrual is going steadily although somewhat slowly, we have now 47 patients randomized and we need to enrol 144 patients altogether. We hope to complete enrolment in the next 2 years. It will take another year to get the results.

*Thank you very much!*

Dr Martin van den Bent is the study coordinator (along with Dr Ahmed Ibdaih) of the EORTC Brain Tumor Group trial entitled, “A randomized trial assessing the significance of Bevacizumab in recurrent grade II and grade III gliomas. The TAVAREC trial”.

EORTC protocol number is 26091 and EudraCT number 2009-017422-39.

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