Volume 4 (2014) // Issue 3 // e-ISSN 2224-3453

European Association of NeuroOncology Magazine

Neurology · Neurosurgery · Medical Oncology · Radiotherapy · Paediatric Neuro-oncology · Neuropathology · Neuroradiology · Neuroimaging · Nursing · Patient Issues

Ongoing Trials: Interview with Dr. Antonio Omuro, MSKCC, about the RTOG 1114-Phase II Randomized Study of Chemotherapy with and without Low-Dose WBRT for Primary Central Nervous Lymphoma

Abacioglu U

European Association of NeuroOncology Magazine 2014; 4 (3) 130-131

Homepage

www.kup.at/journals/eano/index.html

Online Database Featuring Author, Key Word and Full-Text Search

THE EUROPEAN ASSOCIATION OF NEUROONCOLOGY

Member of the DOAJ

Indexed in EMBASE

Krause & Pachernegg GmbH · VERLAG für MEDIZIN und WIRTSCHAFT · A-3003 Gablitz, Austria

Interview with Dr. Antonio Omuro, MSKCC, about the RTOG 1114-Phase II Randomized Study of Chemotherapy with and without Low-Dose WBRT for Primary Central Nervous Lymphoma

Ufuk Abacioglu

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

Q: *Dr. Antonio Omuro, can you tell us about the ongoing RTOG 1114 Randomized Study of Rituximab, Methotrexate, Procarbazine, Vincristine and Cytarabine with and without Low-Dose Whole-Brain Radiotherapy (WBRT) for Primary Central Nervous System Lymphoma? What is the rationale and background for this trial?*

A: This trial is a follow-up to a single-arm phase II study conducted in the US that used R-MPV (rituximab, methotrexate, procarbazine, vincristine) chemotherapy followed by reduced doses of radiotherapy in patients who achieve a CR, and which found an intent-to-treat median PFS of 3.3 years and OS of 6.6 years; the group that received reduced WBRT achieved a median PFS of 7.7 years, with the median OS not reached after median follow-up of 6 years [1]. Neuropsychological evaluation suggested that these doses of radiotherapy are much safer and less toxic than full doses of radiotherapy. The intent is to confirm the excellent results in a community environment and also to determine whether the efficacy could actually be a result of the improved chemotherapy regimen, which is different from previous studies because of the addition of rituximab, and has never been tested without radiotherapy.

Q: *Can you tell us the background to choose this chemotherapy scheme?*

A: The MPV chemotherapy has been succesfully used for a long time in studies conducted at MSKCC, with favorable results that have been attributed to institutional bias. Other critics of this regimen believe it is highly toxic and uses drugs that do not penetrate well into the brain. However, increasingly, it appears that this regimen is indeed very effective, as suggested by preliminary results of the ANOCEF/ GOELAMS trial conducted in France that showed more favorable results of MPV as compared to methotrexate and temozolomide [2]. We felt MPV would be the optimal backbone to test the low-dose radiotherapy hypothesis, as this radiotherapy will work best in the setting of minimal residual disease after chemotherapy. Rituximab has been added, and nobody knows if it made a difference, but given the favorable results, we decided to keep it as not to change too many variables.

Q: *What are the objectives of this trial?*

A: The primary objective is to determine the PFS in both arms, on an intent-to-treat basis. We will also evaluate quality of life and perform neuropsychological evaluation, and of course look at overall survival and response rates.

Q: *How is the trial designed? What are the eligibility criteria?*

A: This is a randomized phase II study, with a total of 89 patients randomized on a 1:1 basis to receive either R-MPV with versus without low-dose RT. Patients are stratified by the MSKCC RPA class, prior to the chemotherapy. After chemotherapy which includes 8 methotrexate doses, patients either receive low-dose RT followed by cytarabine or cytarabine alone, regardless of their response status.

Q: *What do you mean by Low-Dose Radiotherapy, and can you compare the dose within the previous trials?*

A: Our regimen consists of WBRT given at a total dose of 23.4 Gy in 13 fractions. Previous work on MPV has used doses of 45 Gy, but very high neurotoxicity rates were seen. In the literature, WBRT doses are all over the place, ranging from 36–60 Gy, but characterization of neurotoxicity is difficult because each study defines and reports it in one way.

Q: *Which groups and how many centers participate in the trial?*

A: This is a study being conducted by the NRG (former RTOG), which is a cooperative group sponsored by the NCI. There are currently 81 activated sites across the USA.

Q: *Do you have any translational research, quality of life and cognitive function assessments in the study?*

A: Yes, all patients are followed with neuropsychological evaluation and quality of life for 5 years, regardless of tumor progression. If we have more relapses in the chemotherapy arm and similar survival, we will be able to find out in the aggregate results if it is best to have reduced dose RT up front, or let the disease relapse and use salvage treatments, which can also cause cognitive deterioration. We are also collecting tumor specimens with the intent of performing DASL-based gene expression studies for molecular characterization of PCNSL, as well as radiographic images and blood to look for polymorphisms predicting toxicity to methotrexate and radiotherapy.

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

A: We have already accrued 51 patients, and we expect to complete enrollment in 12–18 months. We are hoping to present the first results by 2016.

Thank you very much!

Dr. Antonio Omuro *is the study coordinator for the trial entitled "RTOG 1114 Phase II Randomized Study of Rituximab, Methotrexate, Procarbazine, Vincristine and Cytarabine with and without Low-Dose Whole-Brain Radiotherapy for Primary Central Nervous System Lymphoma".*

Contact Details:
Dr. Antonio Omuro, Associate Professor
Department of Neurology,
Memorial Sloan-Kettering Cancer Center
1275 York Avenue, New York, NY, USA 10065
e-mail: OmuroA@mskcc.org

References:

1. Morris PG, Correa DD, Yahalom J, et al. Rituximab, methotrexate, procarbazine, and vincristine followed by consolidation reduced-dose whole-brain radiotherapy and cytarabine in newly diagnosed primary CNS lymphoma: final results and long-term outcome. J Clin Oncol 2013; 31: 3971–9.

2. Omuro A, Chinot O, Taillandier L, et al. Multicenter randomized phase II trial of methotrexate and temozolomide versus methotrexate, procarbazine, vincristine and cytarabine for newly-diagnosed primary CNS lymphoma (PCNSL) in the elderly: an ANOCEF / GOELAMS Intergroup study. SNO meeting, 2013; N0-107.

Correspondence to:
Ufuk Abacioglu, MD
Department of Radiation Oncology
Neolife Medical Center
Yucel Sok # 6
1. Levent, Besiktas
34340 Istanbul
Turkey
e-mail: ufuk.abacioglu@neolife.com.tr