EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

Roger Stupp, MD
President, EORTC

UNIVERSITAETSSPITAL
Raemisstrasse 100
CH-8091 Zurich
Switzerland
Phone: +41-44-255-9779

Email: roger.stupp@usz.ch

Dr. Martin Hutchings
RIGSHOSPITALET
Blegdamsvej 9
DK 2100 Copenhagen 2100
Denmark

Email: hutchings@dadlnet.dk

Brussels, 6 March 2014

Our Ref. : RS/lge

Re: Very early FDG-PET/CT-response adapted therapy for advanced stage Hodgkin Lymphoma (H11), a randomized phase III non-inferiority study.

Dear Dr. Hutchings, dear Martin:

Thank you for your mail, and congratulations for obtaining additional support from the Dutch Cancer League (KWF).

As you know, the Board has repeatedly and extensively considered your trial. To our great regret we had to come to the conclusion that the trial initially designed over 4 years ago does not answer a sufficiently relevant question anymore, and in particular the question already partially answered by other trials today will have no impact anymore at the projected trial analysis in approx. 8 years.

The Board made its decision on scientific grounds, further accentuated by the absence of any recruitment after 5 sites have been opened to recruitment for more than 3 months, one of them for more than 6 months. The financial considerations were of the least importance. The Board has great doubts on the relevance of the question, the challenges of patient recruitment and the long duration.

Please find below a few of the Board's considerations (non-exhaustive):

In our humble opinion, the value of PET has been investigated in Hodgkin's disease repeatedly, albeit in part using other treatment regimens or performing the early PET after 2 cycles rather than after 1 cycle.

Engert et al. showed the excellent negative predictive value of PET in advanced disease, treated with BEACOPPesc. (Engert et al. Lancet 2012; 379:1791). Early PET after 2 cycles of ABVD is investigated in the RATHL trial conducted by the NCRI. Similarly, the FIL-HD-0801 trial are escalating the therapeutic approach in case of PET positivity after 2 cycles of ABVD. Lastly, the HF0607 trial will stratify patients according to early PET after 2 cycles of ABVD, then investigate transplant strategy and 2 different regimens of BEACOPP or ABVD. It shows an overall survival of > 88% for patients who remained PET pos. after the first 2 cycles of BEACOPP. Last but not least, brentuximab and other monoclonal antibodies and targeted therapies are about to change the disease management, hence questioning the relevance of the trial. It is critical that as an academic organization, we consider timeliness of our trials in a fast changing environment.

./..

While this trial had value when it was designed, it should have been conducted in the immediate following years.

We do understand and recognize that the question on the superiority (or lack thereof) of BEACOPP escalated (popular in Germany) versus ABVD (USA) remains heavily disputed, we recognize that BEACOPP escalated is more toxic than ABVD, and that risk adapted strategies are of importance. Nevertheless, if there is a difference between the 2 regimens, this is likely to be fairly small, can in part be counterbalanced by effective salvage therapy and both treatment regimens will be replaced or complemented by an anti-CD30 treatment in the years to come.

Recruitment of over 500 patients is needed by approx. 40 sites (if all get activated), when the few sites already active were unable to recruit a single patient in > 6 months.

As previously indicated, 300.000 Euros will be saved from the allocated academic fund to the survivorship program of the group. The rest of the academic fund cannot be earmarked for the group as a fair attitude towards the rest of the EORTC network and in accordance with the same rule which had been applied to other groups in a similar situation.

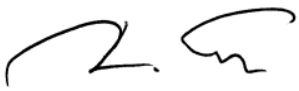
Conclusion:

The trial as proposed and outline approved in 2011 (3 years ago) is by its current design neither feasible nor sufficiently relevant to be pursued for almost another decade. The EORTC HQ will proceed to the closure of the trial. The group is invited to revisit their strategy and protocol, and strongly encouraged to join forces with one of the ongoing trials by other cooperative groups (this way at least some questions get answered).

I hope this clarifies some of your questions. Be reassured that we considered our decision carefully, and we trust that this is in the best interest of the group and the organization.

We thank you for the understanding, and we regret that we have to disappoint you. We will be happy to help the group moving forward with more appropriate projects.

Sincerely yours,



On behalf of the EORTC Board

Roger Stupp, MD
EORTC President