

A multicentre phase III open-label randomized study in patients with advanced follicular lymphoma evaluating the benefit of maintenance therapy with rituximab after induction of response with chemotherapy plus rituximab in comparison with no maintenance therapy.

Cut-off date (14-JAN-2009) for Interim Analysis has been reached!
259 PFS Events reported to GELARC on 04-FEB-2009.

Topics

- Interim Analysis - Timelines
- New CRF pages
- CRF Completion
- Protocol Amendment # 4
- Adverse Events Reporting
- CT Scan Collection Status

Interim Analysis - Timelines

Based on the 259 PFS Events reported and entered in the Database, the timelines for the Interim Analysis have been defined as in the table below. In order to comply with these tight timelines, it could be necessary that Ad Hoc monitoring visits need to be performed at some sites. The CRA will stay in contact with you, in order to plan the corresponding adjustments.

We thank you in advance for your support and collaboration!

TASK DESCRIPTION	TASK DURATION*	Timeline
Clinical Cut-Off for IA (258th event)	0 days	14-Jan-2009
Last CRF page received at GELARC	10 days	17-Feb-2009
Last GELARC query sent	5 days	2-Mar-2009
Last Coding Query sent by GELARC	-	6-Mar-2009
Last GELARC query resolved by fax + entered	12 days	18-Mar-2009
Last CT Scan sent to Bio-Imaging	2 months	18-Mar-2009
Last GELARC re-query sent	5 days	25-Mar-2009
Last GELARC re-query resolved by fax + entered	8 days	6-Apr-2009
Last Roche science queries sent by GELARC	18 days	30-Apr-2009
Last Roche science queries returned by fax to GELARC and entered	6 days	11-May-2009
Last GELARC/Roche re-queries sent	3 days	14-May-2009
Last GELARC/Roche re-query to GELARC + entered	3 days	19-May-2009
Final Query sent by GELARC (Following GELARC/Roche listing review)	21 days	17-Jun-2009
Final query resolved by fax + entered (following GELARC/Roche listing review)	1 day	18-Jun-2009
Last Investigator CRF signature obtained	-	18-Jun-2009

* Days = Working days

New CRF Pages

Two new CRF pages have been created and will be distributed soon:

1. **Follow-up of Survival Status at day of Cut-off date**. This page needs to be completed for all patients which have not had a visit to the site from 14-OCT-2008 to 14-JAN-2009 (both days inclusive), in order to collect survival status information as per protocol requirement.
2. **Signature Page for Interim Analysis**. This page needs to be signed by all investigators and for each patient, before database closure, in order to ensure that all data to be used for the Interim Analysis is accurate and complete.

Detailed instructions will be provided together with these two pages.

Please be reminded that all queries should be resolved within few days after arrival, in order to allow the CRA to perform Source Data Verification and to collect them during the next Monitoring Visit.

CRF Completion

Toxicity pages must be collected for the interim analysis, even if not completed for all visits. The CRAs have been instructed on the appropriate process and will clarify any questions during the monitoring visits or before, if necessary. If the page was not complete by the time it is collected by the CRA (e.g. not all visits covered on the page have been performed), a photocopy of this page will be collected. **Important action for the site staff**: in the lowest part of the toxicity pages, the box YES or NO for OTHER toxicities must be ticked on the original pages, before the photocopy is made, and resembling the information available up to the cut-off date (14-JAN-2009). Once the page is completed at the next corresponding visit, if something has changed, then a correction (signed and dated) must be done on the original CRF.

Protocol Version 5.1 – 04-DEC-2008 (Amendment # 4)

This Protocol Amendment has been distributed to all countries for submission or notification to Health Authorities/Ethic Committees.

Submission and Approval process is currently ongoing in all countries.

Adverse Events Reporting

Real time reporting of Adverse Events (AE) is required in this study as data are **reviewed on an ongoing basis by Data Safety Monitoring Committee (DSMC)**.

Please do not delay reporting of AEs, even incomplete CRF AE pages (e.g. missing end date) are processed and follow up information can then be reported on the **Complementary Information of Adverse Event** CRF page (pages 58-61).

A new version (5.0) of the CRF Verification Guidelines has been distributed. This document must be signed by all investigators.

CT Scan Collection

Once a patient has received subsequent treatment after progression, no further CT Scans are needed for Bio-I maging.

Last CT scan occurred prior to and including January 14, 2009 will have to be sent to Bio-I maging by March 18, 2009 at the latest. Please also note that it is important to continue to send in all scans that have occurred after the interim analysis cut off.

Reminder: All Bio-I maging DCFs must be answered and sent to Bio-I maging within 5 days after being received.

In case of questions regarding CT Scan collection, please contact the CRA of the Study. He/She will help you or will contact the most appropriate person at Bio-I maging / GELARC / Roche, in order to find an answer/solution to your question.

CT Scan Collection Status - February 10th, 2009

Please ensure that all patients sign the ICF related to Protocol version 4.0 in order to be allowed to collect their CT Scans. Furthermore, all outstanding CT Scans must be submitted to Bio-Imaging as soon as possible.

Countries highlighted in red represent the top countries with higher number of missing CT Scans, Queries and/or patients. Immediate actions for collection of outstanding data should be implemented in these countries.

Country	Number of randomised patients	Consent to CT scan collection			Number of patients received	Number of patients missing	Timepoints (TP) received	Timepoints missing up to 14Jan2009	Unresolved queries
		yes	no	outstanding					
Argentina	13	13	0	0	13	0	78	3	7
Australia	112	107	5	0	105	2	672	83	26
Belgium	63	57	5	1	50	7	326	117	19
Brazil	12	12	0	0	12	0	78	0	7
China	6	6	0	0	6	0	36	4	0
Colombia	5	5	0	0	5	0	29	6	3
Croatia	7	7	0	0	7	0	44	1	12
Czech Republic	30	28	2	0	28	0	251	6	7
Denmark	43	42	1	0	42	0	287	4	0
Finland	22	22	0	0	22	0	136	1	2
France	543	519	23	1	520	0	3148	567	97
India	9	7	2	0	7	0	51	0	0
Israel	8	8	0	0	8	0	46	1	0
Netherlands	14	11	3	0	9	2	45	12	9
New Zealand	22	21	1	0	21	0	124	11	2
Peru	9	7	2	0	7	0	48	4	0
Portugal	16	16	0	0	16	0	105	0	0
Serbia	6	5	1	0	5	0	18	11	17
Spain	37	36	1	0	35	1	195	34	27
Thailand	11	11	0	0	11	0	81	4	0
Turkey	6	6	0	0	6	0	40	0	0
UK	14	14	0	0	14	0	66	10	0
Uruguay	3	3	0	0	3	0	17	0	0
Venezuela	8	8	0	0	8	0	53	5	1
Total	1019	971	46	2	960	12	5974	884	236

PLEASE REMEMBER

1. During Maintenance period with or without Rituximab, patient must have clinical visits every 8 weeks. It is critical to maintain this evaluation as planned in the protocol to avoid any biases between the 2 arms. Refer also to DSMC feedback letter distributed early last year.
2. After 24 months maintenance period the Evaluation at the End of Treatment forms (CRF pages 34, 35, 36) need to be completed independently of how many visits have been done.
3. If a patient is withdrawn due to Treatment Toxicity (AE or SAE reporting action taken with study drug as *discontinued*) the withdrawal page needs to be completed as soon as possible, with reason due to toxicity.

IN CASE OF QUESTIONS

Medical questions: please contact

- Prof. Gilles Salles at GELA
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- Delphine Germain at GELARC
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- Bouchra Benettaib at Roche
(bouchra.benettaib@roche.com or +41 61 687 46 98)

Data Management questions: please contact

- Laurence Girard
(laurence.girard@gelarc.org or +33 4 72 66 93 33)
- Delphine Germain or your DM at GELARC

SAE questions: please contact

- Larissa Mege at GELARC
(larissa.mege@gelarc.org)

THANK YOU FOR YOUR CONTINUOUS SUPPORT AND COMMITMENT!