

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

Last patient has been randomized on November 22nd, 2007.
1030 out of 1217 registered patients have been randomised.
 Thank you all for your work and support!

Status: 1217 patients registered

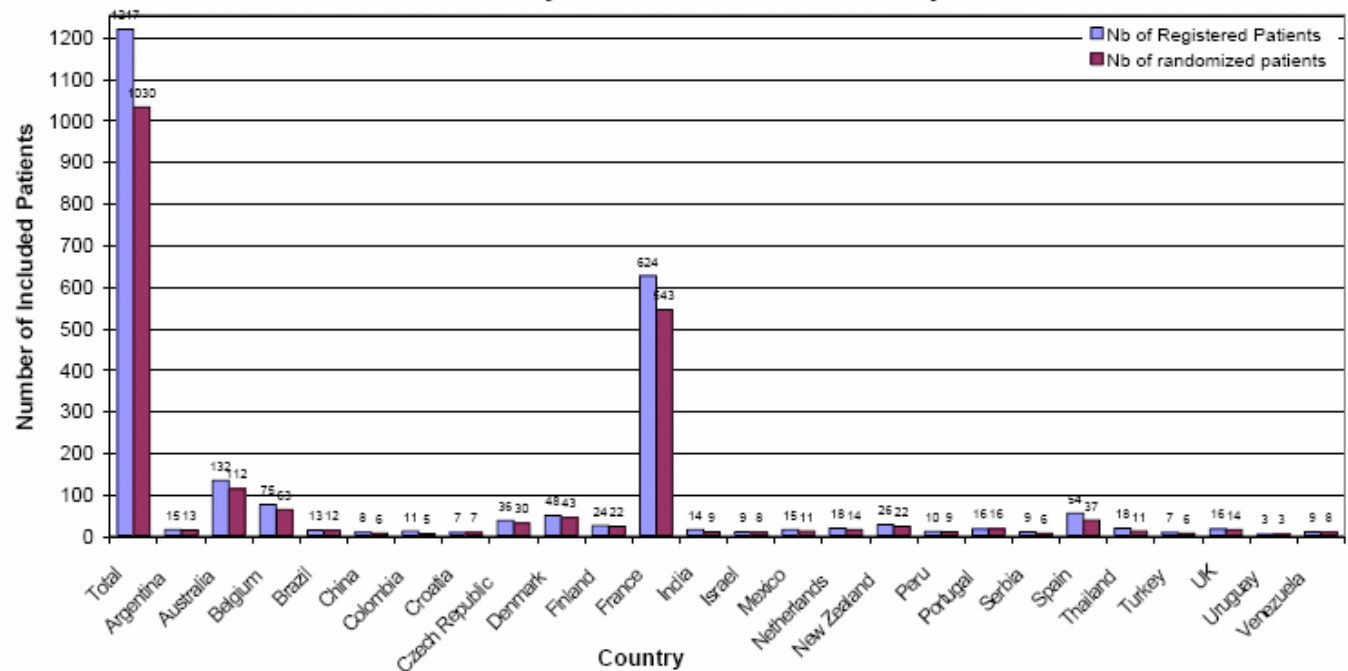
Induction treatment allocation :

- R-CHOP : 900 patients
- R-CVP : 272 patients
- R-FCM : 45 patients

Randomized: 1030 patients

- Maintenance with Rituximab : 513 patients
- Observation : 517 patients

Country Recruitment - PRIMA study



Drug Destruction Process

According to the current Roche SOP for IMP Management, a new process for Drug destruction has been put in place. This process will facilitate your work, and in general it can be divided in two groups, depending on where the drug is destroyed:

1. If drug is destroyed at Roche Warehouses, following documents are required:
 - a. Drug Accountability documentation: e.g. Inventory/Dispensing Log (gcp_for000875)
 - b. IMP Return Form PD 101 (gcp_for000864)
2. If drug is destroyed at investigational site, following documents are required:
 - a. Drug Accountability documentation
 - b. On-site IMP Destruction Form
 - c. A Memo from the site explaining the local process of how the study drug will be destroyed.
 - d. Authorization for On-site IMP Destruction

The CRA need to collect the Memo (2.c) from the site and send it to Alexia Richard (GSL), Norma Hilti (GSOM) or Ramon Aguiar (GSOM). The GSL will review this document and if the process described is according to GCP and Roche standards, the authorization for IMP Destruction (2.d) will be provided. Once this Authorization has been received, it must be archived at the site, and the IMP can be destroyed on an ongoing basis.

A sample Memo (2.c) will be provided. This can be used as template.

Monitoring Reminders

- ✓ **Study Teams contacts:** Any changes should be communicated immediately to **BOTH GELARC and Roche Basel!!** **This is also applicable to Site contact changes.**
- ✓ Please remember to plan and agree the next monitoring visit date with the Investigator at each visit.
- ✓ All Site Closures need to be approved by GELARC. All regulatory documents, acc. to Monitoring Plan, must be previously collected.
- ✓ Please remind investigator:
 1. to obtain all applicable ICF version signed by all patients. Signature dates must be recorded on CRF page 1 and/or 1-2. This page must be then SDVed and sent to GELARC.
 2. that 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. that if a patient is withdrawn due to Treatment Toxicity (AE or SAE) the withdrawal page needs to be completed as soon as possible, with reason due to toxicity.

CT Scan Collection Update by Bio-Imaging

The CT Data Collection for the Roche/GELA PRIMA study is well under way! Bio-Imaging is asking you for your continued assistance as we continue our efforts towards collecting all available CT data.

Prospective CT Scan collection will be started as per January, 2008.

Our team at Bio-Imaging is here to assist you with the data collection. Please let us know how we can assist and we will ensure that your needs are met.

FAQ:

Q: What type of digital data is acceptable at Bio-Imaging?

A: Any digital data should be submitted in uncompressed DICOM format. This is the most widely used format of imaging data. JPEG and TIFF format can NOT be used!

Q: Only film data is available for a patient. How do I submit these data?

A: Film data can be submitted to Bio-Imaging. Upon receipt the data will be digitalized by Bio-Imaging. If only original film data is available and this needs to be returned to the site please tick the "Check box only if films need to be copied and returned to your site" on the Data Transmittal Form. The films will be copied and returned as soon as possible.

Q: I can not locate a randomized patient on the outstanding data spreadsheet. Can I submit the collected data?

A: The outstanding data spreadsheet is updated on a monthly basis and the patient will probably appear on the next list. However, the data can be submitted to Bio-Imaging as long as you make sure that the randomized patient has signed ICF versions 2.0/2.1 and the site has approved protocol amendment 3.

Questions or concerns: Please contact Ryan Cella (rcella@bioimaging.com), Marieke van der Kooi (mvdkooi@bioimaging.com), Rianne Vincenten (rvincenten@bioimaging.com), and/or Karen Kubacke (kkubacke@bioimaging.com).

Safety Reporting and Safety Queries

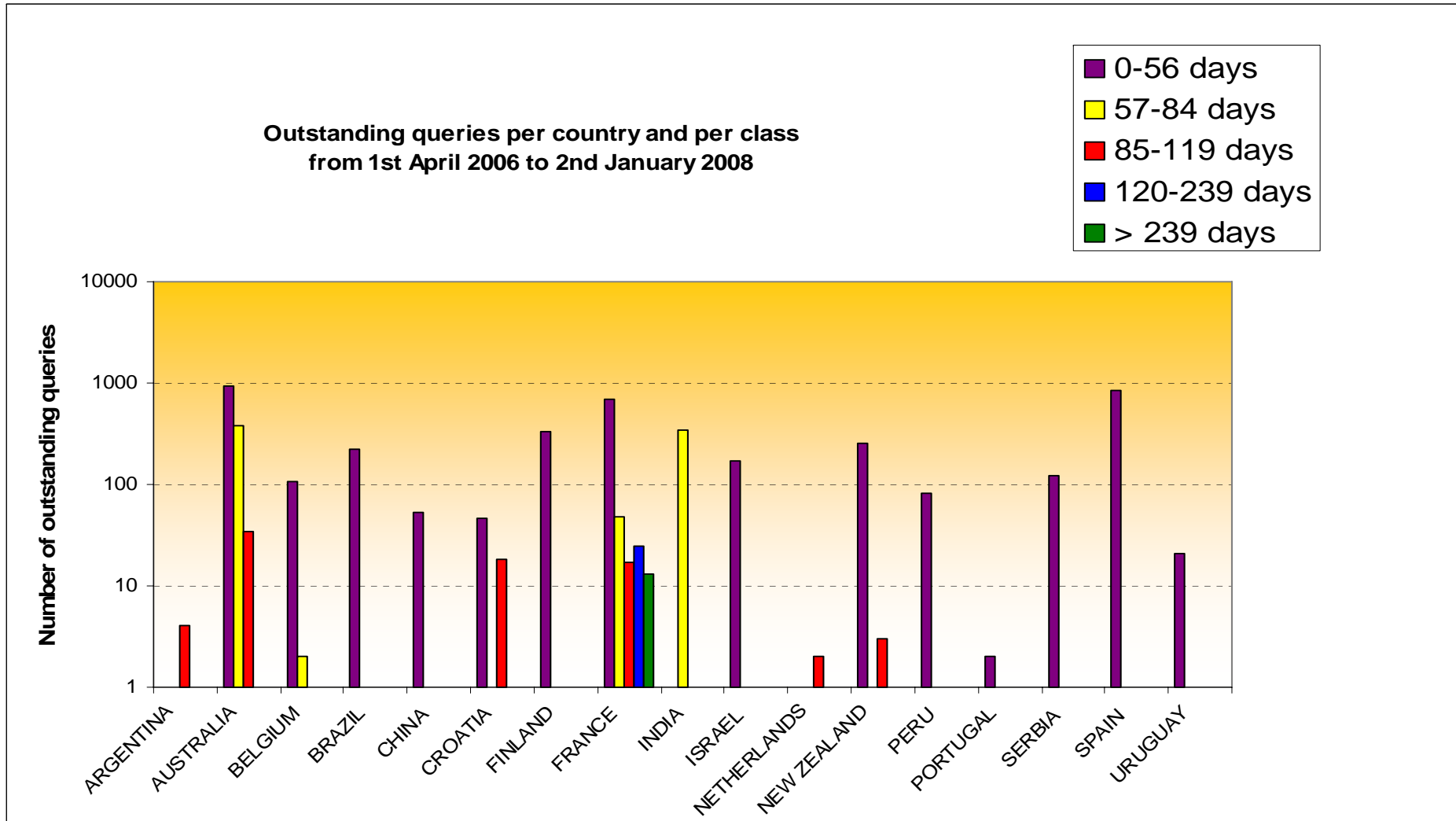
Please remind the investigators that all information submitted to GELARC Safety Desk in a SAE report must be also reflected in the corresponding CRF page and in the Medical Charts of the patient. If the answer to a query related to an SAE report would affect the information reported in the CRF, please ensure that the CRF is amended accordingly.

When performing SDV, please refer to the PRIMA SAE reporting guideline distributed during the last week of November 2008, for detailed information on how the SAE report forms must be filled. Below, you can find the most important points to be considered:

1. Only a single diagnosis must be recorded per report.
2. All the PRIMA study drugs must be listed as study trial medication for both induction and maintenance. Start date is the date of the patient's 1st cycle during induction. Last date before SAE is the date of the last drugs administration before SAE occurred.
3. Relationship to study drugs should always be filled for all study drugs for both induction and maintenance for the SAE to be processed (relationship can always be changed at a later time point with an updated report).
4. All new information is to be updated on a SAE Follow-up form - corresponding CRF AE page must be updated. Be careful to tick off "follow up" for the follow up reports, and "initial" for the initial reports.
5. When you require cancellation of an SAE report, the report must be crossed-out, dated and signed by the investigator, and a reason for cancellation must be given (comment).
6. All the relevant medical information (e.g., medical history, concomitant condition, laboratory results, clinical course of the event) must be indicated in the "comments". Note: Only information entered on an SAE form is processed, attached hospital/lab reports are not considered.

Following items must be equal in both the AE CRF Page and in the SAE report: Patient Number, Date of Birth, Diagnose (Verbatim), AE Onset Date, Outcome, & Relationship to Study Drug (the worse relationship from the SAE report must be recorded on the AE corresponding page)

Please be reminded that all queries should be solved 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.



DSMC Meeting

The PRIMA Data Safety Monitoring Committee (DSMC) has met on **December 2007** during the ASH Congress. Demographic and Safety data of the PRIMA Trial has been reviewed and evaluated during this meeting. An official communication from this meeting will be distributed soon by GELARC.

Based on DSMC Feedback, a priority list of patients has been created. **All outstanding DCFs and CRFs** from the following patients must be collected until January 31st, 2008:

Patients with

1. Study Events (Disease Progression / Death during maintenance)
2. SAEs during maintenance
3. Withdrawal during Maintenance
4. End of Treatment

List of priority patients has been distributed in the week of January 14th, 2008 to all monitors.

Next DSMC meeting is planned for June 2008.

News

- ✓ A CRA Safety Training will be provided by GELARC during the next Country TC on February 13th/14th, 2008. **This training is mandatory for all CRAs.**
- ✓ A new Monitoring Workshop is planned for May/June 2008. Accurate dates and instructions will be provided soon.

Importance of Immediate Events Reporting

Please remind the investigator that **Death or Progression/Relapse pages (pages 47, 47-2, 48 and 49)**, if applicable to the patient - need to be faxed to GELARC **(FAX +33 4 72 66 93 71)** as soon as the Investigator is informed. These pages must be SDVed and collected during the next monitoring visit.

Contact Details

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