2. STUDY SYNOPSIS

Name of Sponsor: Biogen Idec Inc./ Biogen Idec Ltd.	**Individual Study Table Referring to Part <> of the Dossier** **Volume:** **Page:**	***(For National Authority Use only)***
Name of Finished Product: galiximab (IDEC-114)	**Name of Active Ingredient:** galiximab (IDEC-114)	**Study Indication:** Non-Hodgkin's Lymphoma

Title of Study: A Phase III, Open-Label, Multicenter, Single-Arm, Retreatment Study of Galiximab in Combination with Rituximab for Subjects with Relapsed, Follicular Non Hodgkin's Lymphoma who Previously Responded on Study 114-NH-301

Principal Investigator:

- [redacted]

Study Period: Date of first treatment: 09 November 2007 Date of early study termination: 19 October 2009 Date of last subject's last visit: 08 January 2010	**Phase of Development:** III

Study Objectives:

Primary objective:

- To assess the safety of repeat or initial treatment with galiximab in combination with rituximab after relapse in the pivotal Phase III study (114-NH-301).

Secondary objectives:

- To further characterize the pharmacokinetics (PK) of repeat or initial treatment with galiximab in combination with rituximab.
- To further characterize the efficacy profile of galiximab in combination with rituximab.

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Study Design:

This study was originally designed as a Phase III, multicenter, global, open-label, single-arm, retreatment study in subjects with relapsed or refractory follicular non-Hodgkin's lymphoma (NHL) who demonstrated a response on Study 114-NH-301 and a time-to-progression ≥6 months. Subjects were to be enrolled and receive galiximab (500 mg/m^2) in combination with rituximab (375 mg/m^2) once weekly for 4 weeks.

The study period for each subject was to be approximately 2 years. Subjects were to receive rituximab and galiximab on Study Days 1, 8, 15, and 22. The rituximab infusion was to be administered prior to the galiximab infusion. Subjects were to complete scheduled visits until Study Month 24, after which they were to enter into the long-term follow-up period of the study. Subjects were then to be followed every 6 months for continuation of response (if applicable), disease progression, and initiation of subsequent lymphoma therapy. Long-term follow-up was to be continued until the subject died, was lost to follow up, or withdrew informed consent.

Although this was an open-label study, all study personnel were to remain blinded to the subjects' treatment assignment on Study 114-NH-301 (rituximab + galiximab, or rituximab + placebo). Study treatment assignments were to be unblinded when Study 114-NH-301 was completed.

This study was terminated early due to the early termination of Study 114-NH-301. The last subject's last visit occurred on 08 January 2010.

Number of Subjects (Planned and Analyzed):

Planned: Approximately 345 subjects were to be enrolled at 135 investigative sites in Asia, Australia, Europe, and North America.

Analyzed: Sixteen subjects were enrolled at 12 sites in Australia (3 sites), Europe (6 sites), and the United States (3 sites). All 16 subjects received treatment and were included in the Safety Population.

Study Treatment, Dose, Mode of Administration:

Galiximab was to be administered weekly by IV infusion at a dose of 500 mg/m^2 for 4 weeks.

Rituximab was to be administered weekly by IV infusion at a dose of 375 mg/m^2 for 4 weeks.

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Duration of Treatment and Follow-Up:

The study period was to consist of screening, registration, treatment, follow-up, and long-term follow-up periods.

Screening: Evaluation of subject eligibility was to be initiated within 4 weeks prior to Study Day 1.

Registration: Registration was to be performed within 1 week prior to Study Day 1.

Treatment period: Rituximab and galiximab infusions were to be administered at the study site once weekly for 4 weeks (Study Days 1, 8, 15, and 22).

Follow-up period: Subjects were to return to the study site for follow-up visits on Study Day 50 and Study Months 3, 6, 9, 12, 15, 18, 21, and 24 (Final Visit).

Long-Term Follow-Up Period: After Study Month 24, subjects were to have entered into the long-term follow-up period of the study, in which they were to be followed by verbal or written contact every 6 months to assess continuation of response (if applicable), disease progression, and initiation of subsequent lymphoma therapy. Subjects were to be discontinued from the study and transitioned into long-term follow-up prior to Study Month 24 if they had initiated subsequent lymphoma therapy with or without disease progression. Long-term follow-up was to be continued until the subject died, was lost to follow-up, or withdrew informed consent.

Results:

Subject disposition:

- Sixteen subjects who demonstrated a response in Study 114-NH-301 were enrolled and treated in this study. Nine of the 16 subjects (56%) had received the rituximab + galiximab combination in Study 114-NH-301 and are identified in the present study as the rituximab + galiximab to rituximab + galiximab (RG-RG) group. Seven of the 16 subjects (44%) had received the rituximab + placebo combination in Study 114-NH-301 and are identified in the present study as the rituximab + placebo to rituximab + galiximab (RP-RG) group.
- All 16 subjects who were enrolled in the study completed the treatment period and were included in the Safety Population.
- All subjects withdrew from the study. The majority of subjects withdrew due to early study termination by the Sponsor.
- Of the 9 subjects in the RG-RG group: 5 (56%) withdrew due to discontinuation of the study by the Sponsor, 3 (33%) withdrew due to disease progression, and 1 subject (11%) died during the study.
- Of the 7 subjects in the RP-RG group: 4 (57%) withdrew due to discontinuation of the study by the Sponsor and 3 (43%) withdrew due to disease progression.

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Demographics and baseline disease characteristics:

- Median age of subjects at study entry was 64 years (range: 28 to 68 years) in the RG-RG group, compared with 62 years (range: 52 to 80 years) in the RP-RG group.
- There were 2 males (22%) and 7 females (78%) in the RG-RG group, compared with 4 males (57%) and 3 females (43%) in the RP-RG group.
- There were 8 Caucasian subjects (89%) and 1 Asian subject (11%) in the RG-RG group, compared with 7 Caucasian subjects (100%) in the RP-RG group.
- The RG-RG and RP-RG groups were similar with respect to baseline disease characteristics. Overall statistics are as follows:
  - Median time since the most recent disease relapse was 2.8 months (range: 0.4 to 15.5 months).
  - Five subjects (31%) had Stage I/II disease, 10 subjects (63%) had Stage III/IV disease, and 1 subject's disease stage was unknown at study entry.
  - Median longest diameter of the largest lesion was 2.85 cm (range: 1.7 cm to 7.5 cm).
  - Follicular Lymphoma International Prognostic Index (FLIPI) risk group classifications were: 7 subjects (44%) were classified as low risk; 4 (25%) were classifed as intermediate risk; and 5 (31%) were classified as high risk..
  - World Health Organization performance status was 0 for 13 subjects (81%), 1 for 2 subjects (13%), and 2 for 1 subject (6%).
  - Five subjects (31%) had bone marrow involvement; 4 (25%) had splenomegaly; and 4 (25%) had hepatomegaly.

Efficacy:

- Seven (44%) of the 16 subjects had a treatment response during the study, including 4 of 9 subjects (44%) in the RG-RG group and 3 of 7 subjects (43%) in the RP-RG group. Of the 9 subjects in the RG-RG group, 1 (11%) had a complete response and 3 (33%) had a partial response to treatment. Of the 7 subjects in the RP-RG group, 1 (14%) had an unconfirmed complete response and 2 (29%) had a partial response to treatment. Additionally, 7 of 16 subjects (44%) had stable disease, including 4 of 9 subjects (44%) in the RG-RG group and 3 of 7 subjects (43%) in the RP-RG group.

Safety:

- A higher incidence of infections was observed in the RG-RG group (4 of 9 subjects, 44%) compared with the RP-RG group (0 of 7 subjects). One of the infections was an SAE of Grade 3 bacterial sepsis that required hospitalization; the others were Grade 2 or less and non-serious. All of these infections resolved and none led to treatment discontinuation. These subjects had

normal or stable hematology parameters, suggesting that their infections had no clear relationship to immunosupression. One subject in the RG-RG group died secondary to hypotension that may have been complicated by septic shock. The event was considered by the Investigator to be unrelated to galiximab.

- A higher incidence of infusion-day AEs was observed in the RG-RG group compared with the RP-RG group. All infusion-day AEs were mild or moderate. The greatest difference was observed on the first infusion day (Study Day 1) with 3 of 9 subjects (33%) in RG-RG group and 0 of 7 subjects in RP-RG group experiencing AEs.
- The overall incidence of subjects experiencing at least 1 AE in the present study (9 of 16 subjects, 56%) was less than that seen in Study 114-NH-301 (272 of 332 subjects, 82%).
- AEs occurring in more than 1 subject included hypotension (3 subjects in the RG-RG group) and upper respiratory tract infection (2 subjects in the RG-RG group).
- The majority of AEs were mild or moderate (Grade 1 or Grade 2) in severity.
- Of the 9 subjects in the RG-RG group: 6 (67%) experienced at least 1 AE, 4 (44%) experienced a galiximab-related AE, and 2 (22%) experienced an SAE. Of the 7 subjects in the RP-RG group: 3 (43%) experienced at least 1 AE, 1 (14%) experienced a galiximab-related AE, and there were no SAEs.
- There were no treatment discontinuations due to AEs.
- No clinically important abnormalities were observed in laboratory test results for blood chemistry, hematology, and urine.

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Conclusions:

- There was a higher incidence of infections and of infusion-day AEs in the RG-RG group compared with the RP-RG group. One infection (Grade 3 bacterial sepsis) required hospitalization and one fatality (hypotension) may have been associated with septic shock. Both occurred in the RG-RG group. All infusion-day AEs resolved and none led to treatment discontinuation. The low number of exposures makes conclusions based on these data difficult; however, there is no clear safety concern from this study that would preclude further study of galiximab and rituximab retreatment after a response with galiximab and rituximab.
- Repeat or initial treatment with galiximab in combination with rituximab was well tolerated in 16 study subjects who had responded to treatment (with galiximab + rituximab or placebo + rituximab) and then relapsed during the preceding Study 114-NH-301.
- Seven of 16 subjects (44%) had a treatment response during the study, including 4 of 9 subjects (44%) in the RG-RG group and 3 of 7 subjects (43%) in the RP-RG group. These data do not suggest a lack of efficacy using galiximab + rituximab as retreatment in subjects who had previously responded to treatment with galiximab + rituximab in the preceding Study 114-NH-301. However, due to the early termination of the present study and resulting small sample size, no further efficacy conclusions could be drawn from the data.

Publications Based on the Study: None

Date of Report: 21 September 2010