Supplementary material

**A Study of Safety and Efficacy of Nivolumab and Bendamustine (NB) in Patients With Relapsed/Refractory Hodgkin Lymphoma After Failure Of Nivolumab Monotherapy.**

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**Figure 1S. Best overall response during nivolumab bendamustine combined therapy**

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**Figure 2S. Event-free survival after nivolumab-bendamustine combination according.**

**Table 1S.The influence of clinical factors on PFS after nivolumab-bendamustine treatment**

|  |  |  |
| --- | --- | --- |
| Grouping variable | Median PFS in strata (HR for Cox regression) | Significance level\* |
| Age | 1.022 | 0.3477 |
| BMI | 1.949 | 0.5509 |
| Best response to nivolumab bendamustine combination (across all groups) | CR: 10.6 mo (95% CI, 6.1-17.5) PR: 9.3 mo (95% CI, 5.5-12.0)SD: Not reached (95% CI, NR-NR)PD: 2.1 (95% CI, NR-NR) IR: Not reached (95% CI, NR-NR) | **0.0001** |
| Best response to Nivolumab monotherapy | CR: 14.2 mo (95% CI, 9.8-NR)PR/SD/IR: 13.0 mo (95% CI, 8.2-NR)PD: 5.9 mo (95% CI, 2.1-9.3) | **0.0230** |
| B-symptoms at study start |  Yes: Not reached (95% CI, 9.3-NR)No: 10.2 (95% CI, 7.6-13.2) | 0.4739 |
| Consolidation of response achieved with combination, other than alloHSCT(no landmark) | Yes: 9.8 mo (95% CI, 5.0-14.2)No: 10.6 mo (95% CI, 7.6-17.5) | 0.3716 |
| Gender | Male: 9.8 mo (95% CI, 6.1-14.2) Female: 10.6 mo (95% CI, 5.5-NR) | 0.6479 |
| Histological variant | NS: 11.2 mo (95% CI, 6.8-14.9)MC: 7.1 mo (95% CI, 4.6-17.5)LD: 8.4 mo (95% CI, 7.6-9.3)LR: NR (95% CI, 14.2-NR) | 0.2580 |
| Nivolumab bendamustine as bridge to alloHSCT(no landmark) | Yes: Not reached (95% CI 5.5-NR)No: 9.8 mo (95% CI, 7.6-13.0) | **0.0189** |
| Number of prior therapy lines | 1.107 | 0.3335 |
| Progression as BOR to nivolumab monotherapy | Yes: 5.9 mo (95% CI, 2.1-9.3)No: 13.1 mo (95% CI, 8.6-NR) | **0.0063** |
| Primary chemoresistance | Yes: 11.3 mo (95% CI, 5.5-17.5)No: 9.8 mo (95% CI, 7.6-14.9) | 0.9841 |
| Prior ASCT | Yes: 11.3 mo (95% CI, 5.6-NR)No: 9.0 mo (95% CI, 6.1-13.2) | 0.4457 |
| Prior bendamustine | Yes: 10.8 mo (95% CI, 6.8-17.5)No: 9.9 mo (95% CI, 5.0-14.2)  | 0.4849 |
| Prior bendamustine refractory | Yes: 11.8 mo (95% CI, 4.6-NR)No: 9.2 mo (95% CI, 5.5-14.9) | 0,1606 |
| Prior BV | Yes: 10.9 mo (95% CI, 5.5-NR)No: 10.2 mo (95% CI, 7.6-13.2) | 0.8155 |
| Prior nivolumab combination | Yes: 9.5 mo (95% CI, 8.6-NR)No: 11.2 mo (95% CI, 6.8-14.2) | 0.9379 |
| Prior radiotherapy | Yes: 9.8 mo (95% CI, 6.8-13.2)No: 12.4 mo (95% CI, 5.0-17.5) | 0.8839 |
| Stage at study start | II: Not reached (95% CI, NR-NR)III: Not reached (95% CI, NR-NR)IV: 9.5 mo (95% CI, 6.8-13.2) | 0.4866 |
| Status at study start | PR: 9.3 (95% CI, 6.1-NR)SD: Not reached (95% CI NR-NR)PD: 9.8 mo (95% CI, 5.6-14.2)IR2: 13.2 mo (95% CI 4.6-17.5)IR3: Not reached (95% CI NR-NR) | 0.9747 |
| Time from prior nivolumab discontinuation to combo  | 0.999 | 0,9352 |
| Time from prior bendamustine discontinuation to combo | 1.000 | 0,8802 |
| Tumor volume before combination | 1.000 | 0.0898 |

\*PFS estimation with Kaplan-Mayer method with test of equality over strata (Log rank test) for nominal variable, Cox regression with analysis of Maximum Likelihood Estimates for interval variable

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**Figure 3S. Progression free survival after nivolumab-bendamustine combination according to anamnesis of prior bendamustine monotherapy.**

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**Figure 4S. Progression free survival after nivolumab-bendamustine combination according to best overall response during therapy.**

**Table 2S. Next treatment after nivolumab-bendamustine treatment**

|  |  |  |
| --- | --- | --- |
| Type of next additional treatment | N | (%) |
| Nivolumab monotherapy | 12 | 40% |
| Allogeneic SCT | 5 | 16,6% |
| Nivolumab-BV combination | 2 | 6,6% |
| Other nivolumab combination | 4 | 13,3% |
| BV monotherapy | 2 | 6,6% |
| Chemotherapy | 2 | 6,6% |



**Figure 5S. Progression-free survival (PFS) in patients with response to nivolumab-bendamustine that received maintenance/consolidation therapy other than alloHSCT vs. other patients.**

**Table 3S. Structure of observed immune related adverse events**

|  |  |  |  |
| --- | --- | --- | --- |
| Type of irAE | irAE overall | irAE Gr 3-4 | irAE Gr 1-2 |
| Any | 21 | 70,0% | 3 | 10,0% | 19 | 63,3% |
| Pyrexia | 11 | 36,7% | 0 | 0,0% | 11 | 36,7% |
| Pruritus | 10 | 33,3% | 0 | 0,0% | 10 | 33,3% |
| Rash | 3 | 10,0% | 0 | 0,0% | 3 | 10,0% |
| ALT increased | 3 | 10,0% | 0 | 0,0% | 3 | 10,0% |
| AST increased | 3 | 10,0% | 0 | 0,0% | 3 | 10,0% |
| Colitis | 2 | 6,7% | 1 | 3,3% | 1 | 3,3% |
| Infusion reaction | 1 | 3,3% | 1 | 3,3% | 0 | 0,0% |
| Uveitis | 1 | 3,3% | 1 | 3,3% | 0 | 0,0% |