Impact of CD20 Expression on Lunsumio Activity

This article responds to your request for information on the need for CD20 expressing B-cells for the activity of Lunsumio® (mosunetuzumab).

In brief

- Lunsumio is an anti-CD20×CD3 T-cell engaging bispecific antibody that targets CD20 expressing B-cells.
- Lunsumio is broadly active in killing multiple human B lymphoma cell lines with various CD20 expression levels.
- Lunsumio has no effect on CD20 negative cells. Loss of CD20 expression on tumor cells during Lunsumio treatment can lead to acquired resistance to Lunsumio.
- There is no recommendation for measuring levels of CD20 expressions prior to administration of Lunsumio.

Abbreviations

B-NHL=B-cell non-Hodgkin lymphomas

EC50s=half maximal effective concentration

FL=follicular lymphoma

IHC=immunohistochemistry

PAX5=a B-cell-specific activator protein

PD=progressive disease

RR=relapsed or refractory

TDB=T-cell dependent bispecific

Role of CD20 expression in mechanism of action of Lunsumio

Lunsumio is an anti-CD20xCD3 T-cell engaging bispecific antibody that targets CD20 expressing B-cells.[1] It is a conditional agonist in that it only induces T-cell activation, cytokine release, and target cell lysis in the presence of CD20 expressing cells.[2]

Effect of low CD20 expression on activity of Lunsumio

Lunsumio is broadly active in killing multiple human B lymphoma cell lines with various CD20 expression levels, including rituximab-insensitive cell lines with low CD20 expression.[2]

In the pivotal trial of Lunsumio in RR FL, post-hoc biomarker analyses were performed to examine potential associations between CD20 expression at baseline and response.[3] Target CD20 expression by IHC was retrospectively measured in 68 baseline biopsies available for biomarker analysis from 53 responders and 15 non-responders. No association between baseline CD20 expression and response was observed. CD20 was generally high and non-normally distributed. CD20 expression was similar in responders and non-responders. Responses were observed in patients across a range that included low levels of CD20 expression; a minimum of 44% was observed in one responder.[3] The study did not have an exclusion criterion related to CD20 expression.

Sun et al. showed that very low antigen expression level, or very low receptor occupancy is sufficient for CD20-TDB activity and CD20-TDB is active even in the presence of competing CD20-targeting antibodies such as rituximab.[4]

In in-vitro studies conducted during development of Lunsumio, there was no particular correlation between EC50s and CD20 expression in cells where CD20 expression levels were available.[5]

Effect of lack of CD20 expression on activity of Lunsumio

Schuster et al. studied if loss of CD20 expression can lead to resistance to Lunsumio in patients with RR B-NHL.[6] They defined loss of CD20 as ≤5% CD20+PAX5+ cells and assessed the levels of CD20 expression relative to response rates. They found that baseline CD20 expression of ≤5% is associated with lack of response to Lunsumio and concluded that during Lunsumio treatment, loss of CD20 expression on tumor cells is one but not the only mechanism of acquired resistance to Lunsumio.[6]

Sun et al. tested CD20-TDB in dose-response assays across a panel of seven B lymphoma cell lines with various levels of CD20 expression. CD20-TDB had no activity against cells that are devoid of CD20 expression.[4]

Another trial investigated baseline features of early disease progression in pts with RR FL treated with Lunsumio and lenalidomide. Out of the five cases with early progression, one was already CD20 negative at baseline and two rapidly lost their CD20 expression.[7]

Requirement for measuring CD20 expression levels before administering Lunsumio

There is no recommendation for measuring levels of CD20 expression prior to administration of Lunsumio.

References

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