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Mavrilimumab
CAR T Induced Cytokine Release Syndrome

May 2020

Forward Looking Statements

This presentation (together with any other statements or information that we may make in connection herewith) contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 with respect to Kiniksa Pharmaceuticals, Ltd. (and its consolidated subsidiaries, collectively, unless context otherwise requires, "Kiniksa," "we," "us" or "our"). In some cases, you can identify forward looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "goal," "design," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these identifying words. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation, statements regarding our strategy for mavrilimumab; collaborations; potential additional indications to explore; potential market opportunities, differentiation and competitive position; on going, planned and potential clinical trials and other studies; timing and potential impact of clinical data; and regulatory and other communications, submissions, applications and approvals.

These statements involve known and unknown risks, uncertainties, and other important factors that may cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements, including without limitation potential delays or difficulties with our current and planned clinical trials with mavrilimumab; potential inability to demonstrate safety or efficacy or otherwise producing negative, inconclusive or uncompetitive results; potential for changes in final data from preliminary or interim data; potential inability to replicate in later clinical trials positive results from earlier trials and studies; impact of additional data from us or other companies; our reliance on third parties for manufacturing and conducting clinical trials, research and other studies; potential changes in our strategy, operating plan and funding requirements; drug substance and/or drug product shortages; substantial new or existing competition; potential impact of the COVID-19 pandemic, and measures taken in response to the pandemic, on our business and operations as well as the business and operations of our manufacturers, contract research organizations, and other third parties with whom we conduct business or otherwise engage; and our ability to attract and retain qualified personnel. These and the important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (the "SEC") on May 4, 2020 and other filings subsequently filed with the SEC. These forward-looking statements reflect various assumptions of Kiniksa's management that may or may not prove to be correct. No forward-looking statement is a guarantee of future results, performance, or achievements, and one should avoid placing undue reliance on such statements. Except as otherwise indicated, this presentation speaks as of the date of this presentation. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

This presentation also contains estimates, projections, and/or other information regarding our industry, our business and the markets for certain of our product candidates, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, clinical trials, studies and similar data prepared by market research firms and other third parties, from industry, medical and general publications, and from government data and similar sources. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information.

Mavrilimumab: Potential to Advance Clinical Profile of CAR T Cell Therapy

Mechanism	• GM-CSF is a key growth factor and cytokine in autoinflammation and autoimmunity.[1] • Mavrilimumab is a monoclonal antibody inhibitor targeting GM-CSFRα.
Rationale	• Treatment related induction of GM-CSF has been identified through clinical, translational and preclinical studies as a potential key signal associated with side effects of chimeric antigen receptor T (CAR T) cell therapy.[2]
Preclinical and Clinical Data	• Preclinical data suggest the potential for interruption of GM-CSF signaling to disrupt CAR T cell mediated inflammation without disrupting anti-tumor efficacy.[3] • Correlative data from YESCARTA®[4] (axicabtagene ciloleucel) pivotal trials suggest that elevated GM-CSF levels are linked to development of Grade 3+ neurologic events (NEs).[2]
Differentiation	• Mavrilimumab is believed to be the only GM-CSF receptor blocker; other anti-GM-CSF mechanisms inhibit the ligand. • GM-CSFRα blockade potentially prevents pathogenic cells from infiltrating into the target tissue, and suppresses multiple markers of inflammation (e.g., IL-2Rα, IL-6, CRP)[5,6,7] • One currently approved treatment of CAR T induced CRS, data suggest that its use as a prophylactic may increase rates of severe NE.[8]
Development Status	• The safety of mavrilimumab has been evaluated in a Phase 2 trial: Mavrilimumab was dosed in over 550 patients with rheumatoid arthritis through Phase 2b by MedImmune in Europe and achieved prospectively-defined primary safety and efficacy endpoints. • Clinical collaboration with Kite, a Gilead Company, to evaluate the investigational combination of Yescarta and mavrilimumab in relapsed or refractory large B-cell lymphoma. The objective of the trial is to evaluate the effect of mavrilimumab on the safety of Yescarta. Expected to commence a Phase 2 trial in the second half of 2020.

1) Wicks, Roberts, Nature Review Immunology, 2015; Hamilton, Expert Review of Clinical Immunology, 11:4, 457-465; 2) Neelapu et al., NEJM 2017; Sterner et al., Blood 2019; Roberts ZJ et al., Leukemia Lymphoma 2018 3) Sterner et al., Blood 2019 ; 4) Yescarta® is a registered trademark of Gilead Sciences, Inc., or its related companies; 5) De Alessandris et al., J Leukoc Biol. 2019; 6) Sterner et al., Blood 2019; 7) Guo et al., Rheumatology 2017; 8) Locke et al., Preliminary Results of Prophylactic Tocilizumab After (Axi-cel;KTE-C19) Treatment for Patients with Refractory, Aggressive NHL, Poster 1547; CRS = cytokine release s syndrome; NE = neurologic events

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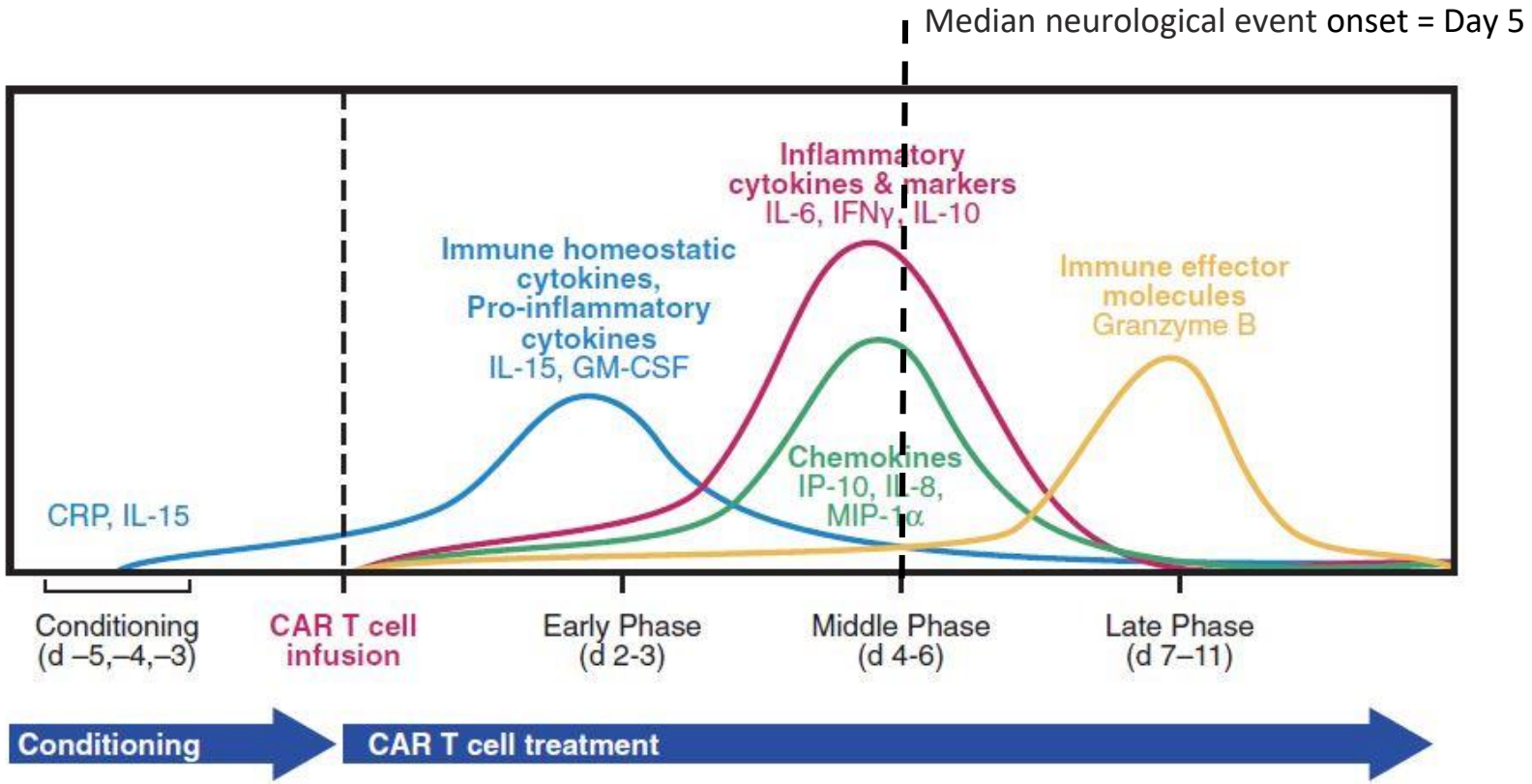
GM-CSF is a Potential Key Signal Associated with Side Effects of CAR T Cell Therapy



Early increases in GM-CSF levels (2-3 days post CAR T cell treatment) is thought to precede and initiate the onset of CRS and NE; therefore prophylactic treatment with mavrilimumab has potential to significantly reduce rates of these severe toxicities[1]

CRS = cytokine release syndrome; NE = neurologic events; 1) Neelapu et al., NEJM 2017; Sterner et al., Blood 2019; Roberts ZJ et al Leukemia Lymphoma 2018

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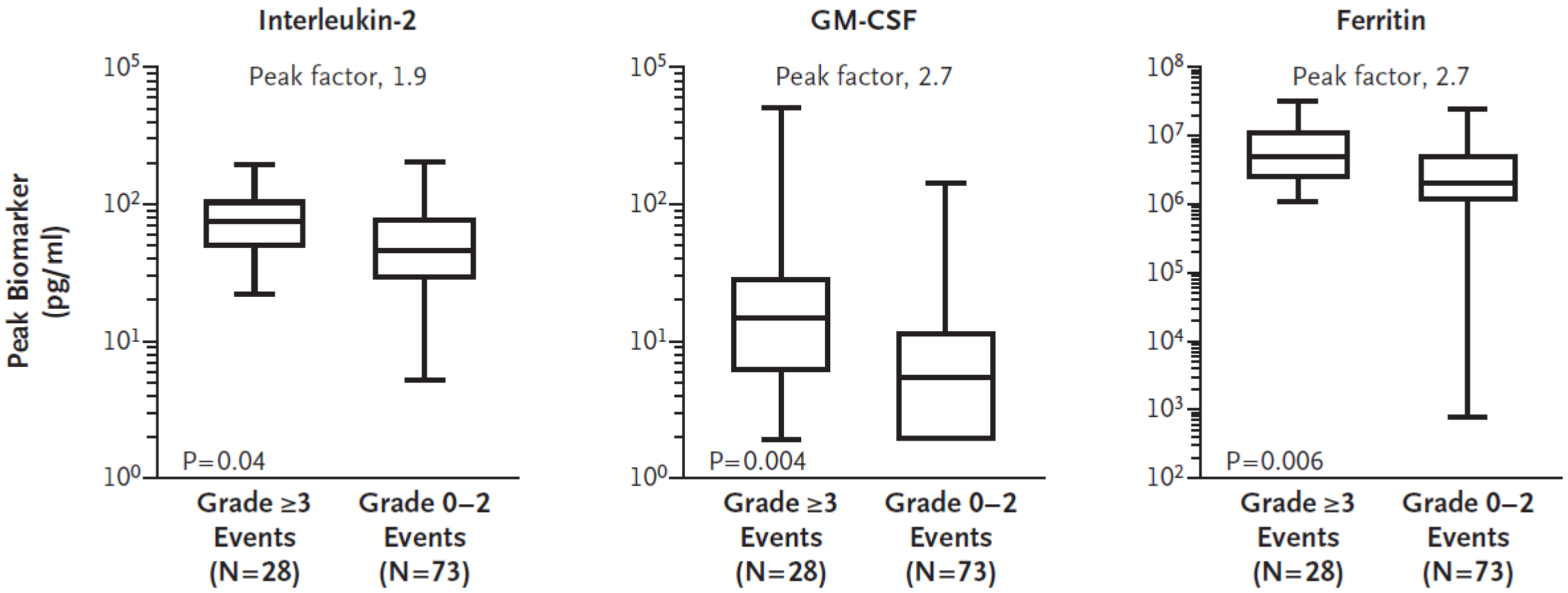
In the ZUMA-1 Trial, Elevated GM-CSF was Most Significantly Associated With the Presence of Severe Neurologic Events in the Biomarkers Explored[1,2]



AUC = area under the curve
CRS = cytokine release syndrome
NE = neurologic events

1) Neelapu et al., Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma, NEJM 2017

2) Peak cytokine levels were used in the comparison. These findings were also applicable to cumulative levels across first 28 days after axi-cel infusion (AUC). Adjusted *P* values are calculated from Holm's procedure after multiple testing using the Wilcoxon rank sum test.

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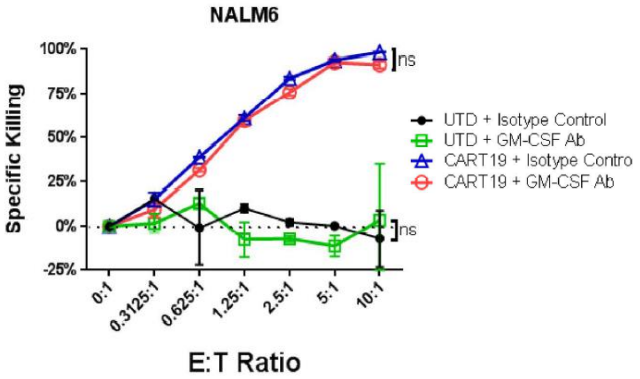
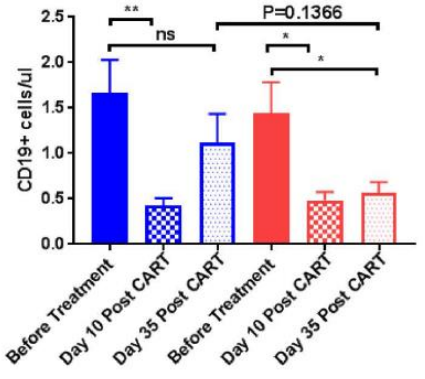
Blockade of GM-CSF signaling attenuated both Cytokine Release Syndrome and Neurologic Events, as well as enhanced CAR T effector function in Preclinical Xenograft Models

GM-CSF Blockade Shows No Negative Effect on CAR T Effector Function

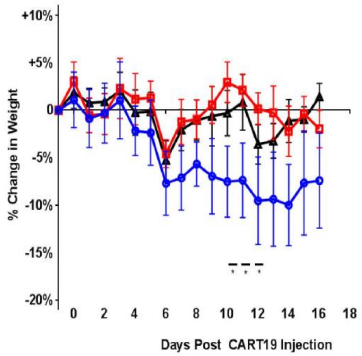




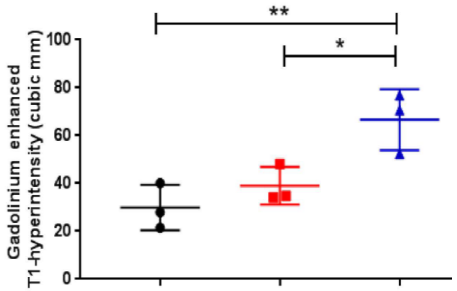
CART19 + anti-GM-CSF showed a more sustained anti-tumor effect than CART19 + control

GM-CSF Blockade Attenuates CRS and Neurological Events

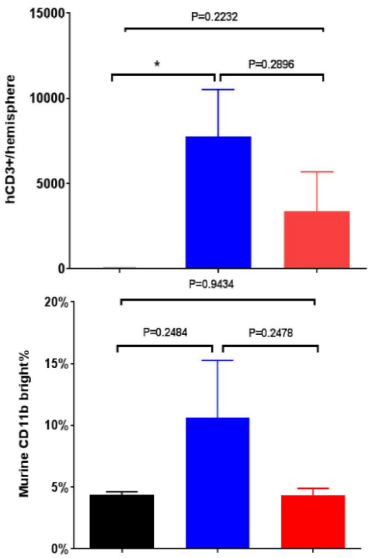
CRS as Measured by Weight Change

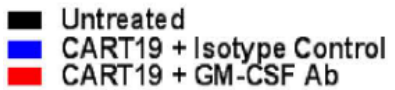


NRS as Measured by Neuroinflammation



NRS as Measured by Cellular Infiltrates





CART19 + anti-GM-CSF treated animals showed reduced CRS (as measured by % change in weight) and NE (as measured by reduction in T1 enhancement and infiltration of T-cells and macrophages)

CRS = cytokine release syndrome
NE = neurologic events
Neelapu et al., NEJM 2017; Sterner et al., Blood 2019

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