NCCN Guidelines Panel: Multiple Myeloma

Submitted by:
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Date of request: April 30, 2019
NCCN Guidelines Panel: Multiple Myeloma

On behalf of SkylineDx, I respectfully request that the NCCN Multiple Myeloma Panel review the existing data and published evidence\textsuperscript{1-17} on the use of SKY92 high risk gene expression signature for patients with either Newly Diagnosed Multiple Myeloma or Relapsed Refractory Multiple Myeloma. SKY92 is a clinically and analytically validated assay marketed in the US by SkylineDx B.V.

Specific Changes

Proposed change for MYEL-4

Specifically we would like to suggest to replace “Bone marrow aspirate and biopsy at relapse with FISH as clinically indicated” with “Bone marrow aspirate and biopsy at relapse with SKY92 and/or FISH as clinically indicated” on page MYEL-4 of Version 2.2019

Statement of whether the submitted use is or is not FDA approved for that indication.

SKY92 is available in the United States as a Laboratory Developed Test (LDT) out of the SkylineDx USA inc. CLIA-licensed laboratory (CLIA #05D2159130) and for which FDA Clearance is not required.

Rationale for recommended change (one sentence).

In the post primary therapy setting we have validation data to show that SKY92 identifies a fraction of patients with significantly shorter PF5 and OS. Namely the APEX dataset (Hazard Ratio 3; p=1.3e-9) and in the TT6 dataset (n=55, Hazard Ratio 10.3; p=7.4e-6) (Table 1).

It seems that the proportion of SKY92 high risk patients increases longitudinally. Thus, a larger proportion of RRMM is at risk for shorter survival. How to clinically interpret this, needs study\textsuperscript{18}.

Proposed change for MS-5 (Discussion Update in Progress)

Specifically, we would like to replace sentence “GEP is a useful tool and may be helpful in selected patients” with this one “SKY92 is a useful tool and may be helpful in NDMM and RRMM patients...”.

Sincerely,

Dharminder Chahal, CEO

April 30, 2019
### Table 1: 14 independent Clinical Validation datasets analyzed with SKY92

<table>
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<th>Cohort</th>
<th>N</th>
<th>High Risk</th>
<th>Standard Risk</th>
<th>Haz Rat OS</th>
<th>p-value</th>
<th>Haz Rat PFS</th>
<th>p-value</th>
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### Citations


8. Rowan Kuiper , Martin H. van Vliet , Mark van Duin , Annemiek Broijl , Mark-David Levin , Leonie de Best , Erik H. van Beers , Bronno van der Holt , Heleen Visser , Markus Hansson , Annette W.G. van der Velden , Belinda Dumee,

9. Martin van Vliet, Joske Ubels, Leonie de Best, Erik van Beers and Pieter Sonneveld. The Combination of SKY92 and ISS Provides a Powerful Tool to Identify Both High Risk and Low Risk Multiple Myeloma Cases, Validation in Two Independent Cohorts. Blood 2015 126:2970


11. Robert Henderson, Mary R Cahill, Philip Murphy, Vitaliy Mykytiv, John Quinn, Jessica Walsh, Elizabeth Lenihan, Tara Kenny, Andres Hernando, Grace Hirakata, Imelda Parker, Emma Kinsella, Grainne Gannon, Alessandro Natoni and Michael E O'Dwyer, Cybord-Dara is a Highly Effective Upfront Treatment for Newly Diagnosed Multiple Myeloma. Initial Efficacy Results of the 16-Bcnl-001/C trial-IE (ICORG) 16-02 Study. Blood 2018 132:3262


17. Rowan Kuiper, Martin H. van Vliet, Mark van Duin, Erik H. van Beers, Pieter Sonneveld. RNA-Seq based risk stratification in multiple myeloma patients validates SKY92 as a high risk marker in the COMMPASS trial EHA 2018 PF528

18. Rowan Kuiper, Erik H. van Beers, Martin H. van Vliet. SKY92 risk stratification at relapse provides additional prognostic information for standard-risk multiple myeloma patients. EHA 2018 Abstract P51295