NCCN Guidelines Panel: Multiple Myeloma

Submitted by:

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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[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 PFS 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[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

	Cohort	N	High Risk	Standard Risk	Haz Rat OS	p-value	Haz Rat PFS	p-value	Reference (hyperlinked)
1	TT2	351	68	283	3,4	5,7e-8			Kuiper 2012
2	TT3	142	23	119	5,2	1,8e-5			Kuiper 2012
3	MRC-IX	247	50	197	2,4	3,6e-6			Kuiper 2012
4	APEX	264	43	221	3,0	1,3e-8			Kuiper 2012
5	MMGI	91	19	72	8,2	1,2e-8			Van Beers 2017
6	HOVON-87/NMSG-18	178	25	153	3,0	1,3e-4			Kuiper 2017
7	E-MTAB-1038	66	13	53	2,6	2,2e-2			Van Vliet 2015
8	TT6	55	11	44	10,3	7,4e-5			Van Vliet 2015
9	MRC-XI	318	78	240	3,9	1,0e-4			Sherborne 2016
10	EMN-02/Hovon95	228	46	182	3,7	<1,0e-3			Hofste 2018
11	KTd (CarThaDex)	49	8	41	3,7	6,0e-2			Wester 2016
12	KRd (Jakubowiak)	39	6	33			8,2	8,5E-3	Van Vliet 2014
13	GIMEMA-MMY-3006 VTD	114	23	91	4,0	1,8e-3			Van Beers
14	CoMMpass	630	115	515	3,3	1,8e-7			Kuiper 2018
	Total	**2772**	**528**	**2244**					

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