Impact of Upstaged Risk by the Molecular International Prognostic Scoring System in Myelodysplastic Syndromes

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Introduction

- The Molecular International Prognostics Scoring System (IPSS-M) considers mutations to refine traditional Revised IPSS (IPSS-R) risk in myelodysplastic syndromes (MDS).
- This results in some patients moving from a lower to higher risk category (upstaging).
- The clinical outcomes and optimal management of upstaged patients are incompletely understood.

Aim

- Evaluate in detail the characteristics and clinical outcomes of patients with MDS and upstaged risk from IPSS-R to IPSS-M.

Methods

- Retrospective chart/database review study from large academic center.
- **Upstaged** patients defined as IPSS-R ≤ 3.5 points and IPSS-M > 0.0 points.
- **Downstaged** patients defined as IPSS-R > 3.5 points and IPSS-M ≤ 0.0 points.
- Other patients classified as **concordant lower risk** (LR: IPSS-R ≤ 3.5, IPSS-M ≤ 0.0) or **concordant higher risk** (HR: IPSS-R > 3.5, IPSS-M > 0.0).
- Landmark analyses to evaluate impact of SCT (median time to SCT as landmark).

Summary

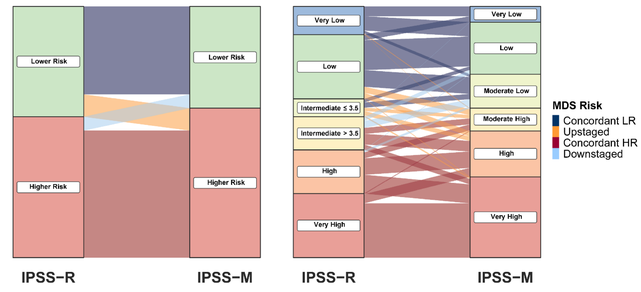
- Patients with MDS upstaged by the IPSS-M experience outcomes similar to *TP53*-wild-type concordant HR MDS. This warrants treating upstaged patients as HR MDS.
- Downstaged patients have favorable OS, but higher incidence of AML compared to concordant LR and appear to benefit from SCT.

Results

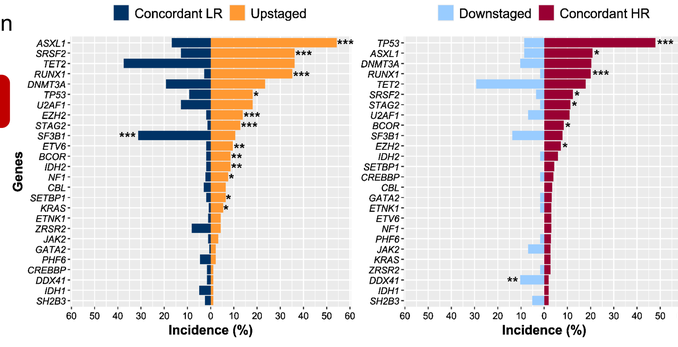
Baseline Patient Characteristics

Variable	Full Cohort n=1054	A: Concordant LR n=369	B: Upstaged n=94	p (A vs B)	C: Concordant HR n=533	D: Downstaged n=58	p (C vs D)
Age	70 [22-94]	69 [23-93]	72 [26-91]	0.005	69 [24-94]	68 [22-83]	0.142
Male	680 (65)	253 (69)	67 (71)	0.708	321 (60)	39 (67)	0.324
Therapy-related	357 (34)	92 (25)	33 (35)	0.052	217 (41)	15 (26)	0.033
Hemoglobin, g/dL	9.4 [3.2-16.4]	10.5 [6.1-16.4]	9.4 [3.2-16.0]	<0.001	8.7 [5.2-14.5]	11.0 [6.7-16.2]	<0.001
Platelets, x 10^9/L	90 [5-807]	151 [15-628]	96 [14-807]	<0.001	59 [5-692]	84 [8-449]	0.011
ANC, x 10^9/L	1.45 [0.03-112.91]	1.98 [0.04-15.98]	1.71 [0.25-35.11]	0.366	1.06 [0.03-112.91]	1.39 [0.22-23.35]	0.083
BM blasts, %	4.0 [0.0-19.0]	2.0 [0.0-12.0]	2.0 [0.0-15.0]	0.002	8.0 [0.0-19.0]	5.0 [1.0-16.0]	<0.001
Cytogenetic risk							
Very Good	28 (3)	23 (6)	3 (3)	0.287	2 (0)	0	<0.001
Good	520 (49)	288 (78)	71 (76)		128 (24)	33 (57)	
Intermediate	157 (15)	49 (13)	15 (16)		81 (15)	12 (21)	
Poor	105 (10)	9 (2)	5 (5)		83 (16)	8 (14)	
Very Poor	244 (23)	0	0		239 (45)	5 (9)	
IPSS-R score	4.0 [0.0-10.0]	2.0 [0.0-3.5]	3.0 [1.0-3.5]	<0.001	6.5 [4.0-10.0]	4.0 [4.0-5.5]	<0.001
IPSS-R risk							
Very Low	118 (11)	113 (31)	5 (5)	<0.001	0	0	<0.001
Low	270 (26)	219 (59)	51 (54)		0	0	
Intermediate	214 (20)	37 (10)	38 (40)		92 (17)	47 (81)	
High	183 (17)	0	0		172 (32)	11 (19)	
Very High	269 (26)	0	0		269 (50)	0	

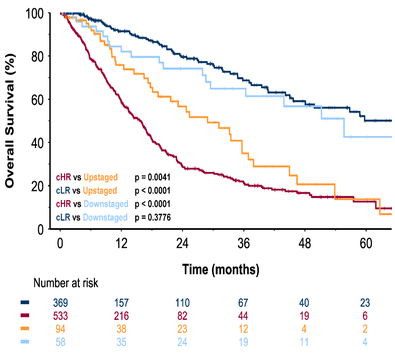
Compared to IPSS-R, IPSS-M led to:
-**Upstaging** in 94 patients (9%)
-**Downstaging** in 58 patients (6%)



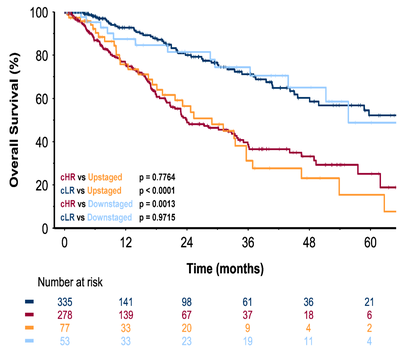
Mutation patterns



OS, full cohort

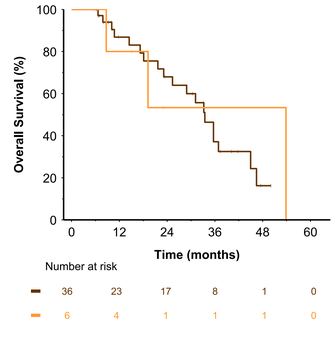


OS, excluding *TP53*-mutated

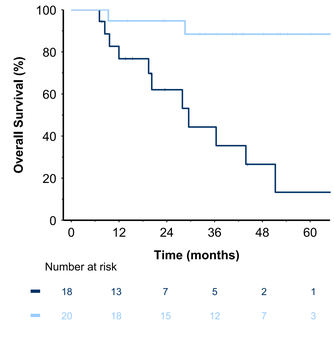


Landmark OS, stratified by SCT

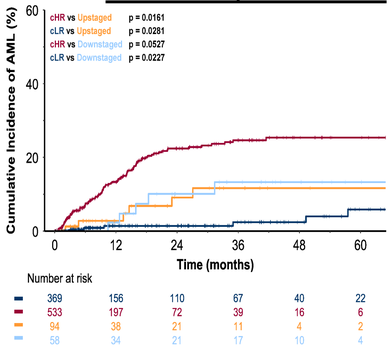
Upstaged patients



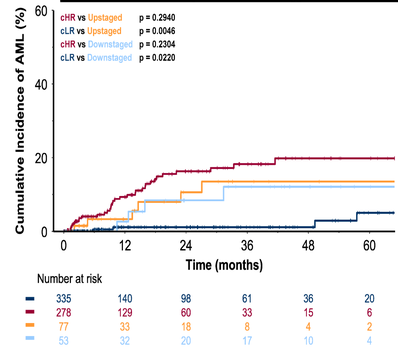
Downstaged patients



CI of AML, full cohort



CI of AML, excluding *TP53*-mutated



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