LETTER TO THE EDITOR

Retrospective cohort study of treatment with BCL-2 inhibitor venetoclax in advanced AL amyloidosis

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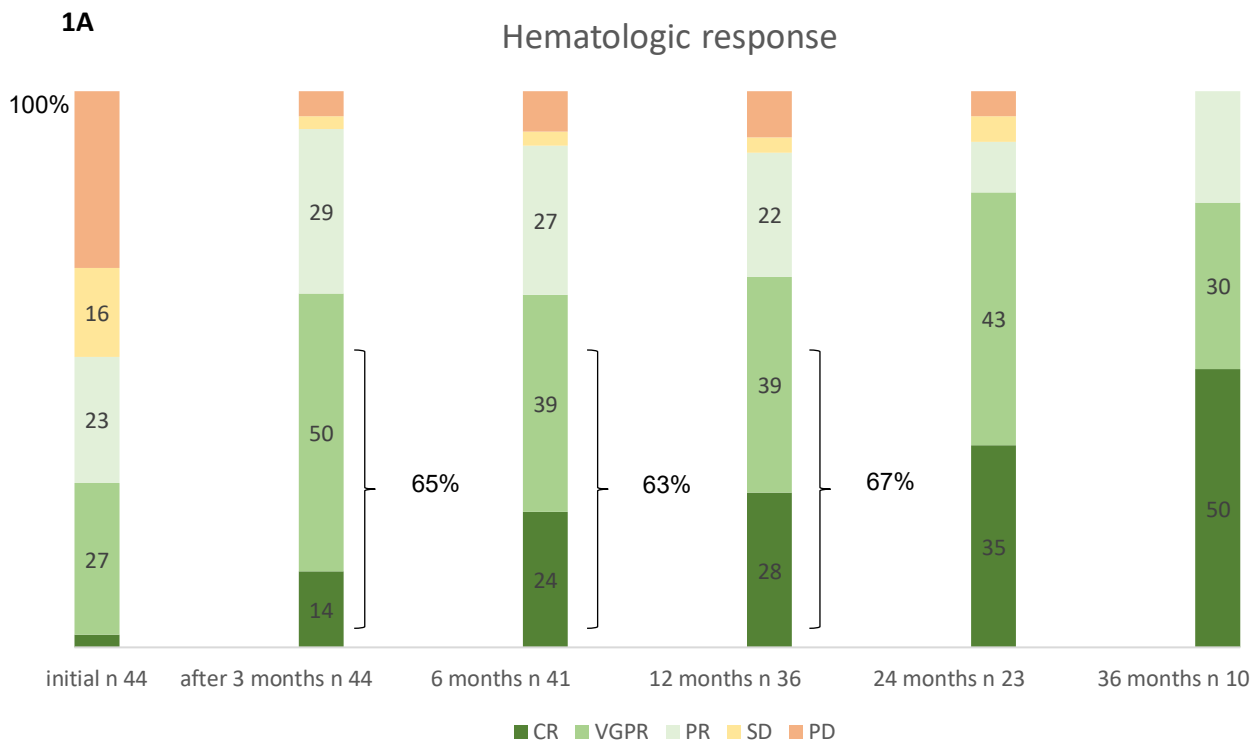
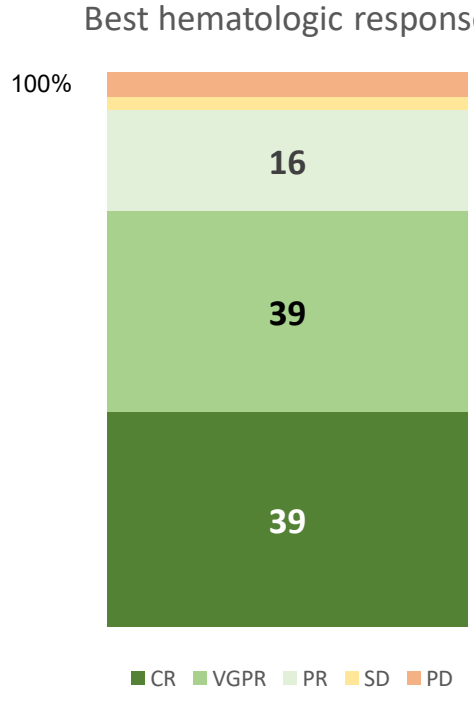
SUPPLEMENTARY DATA

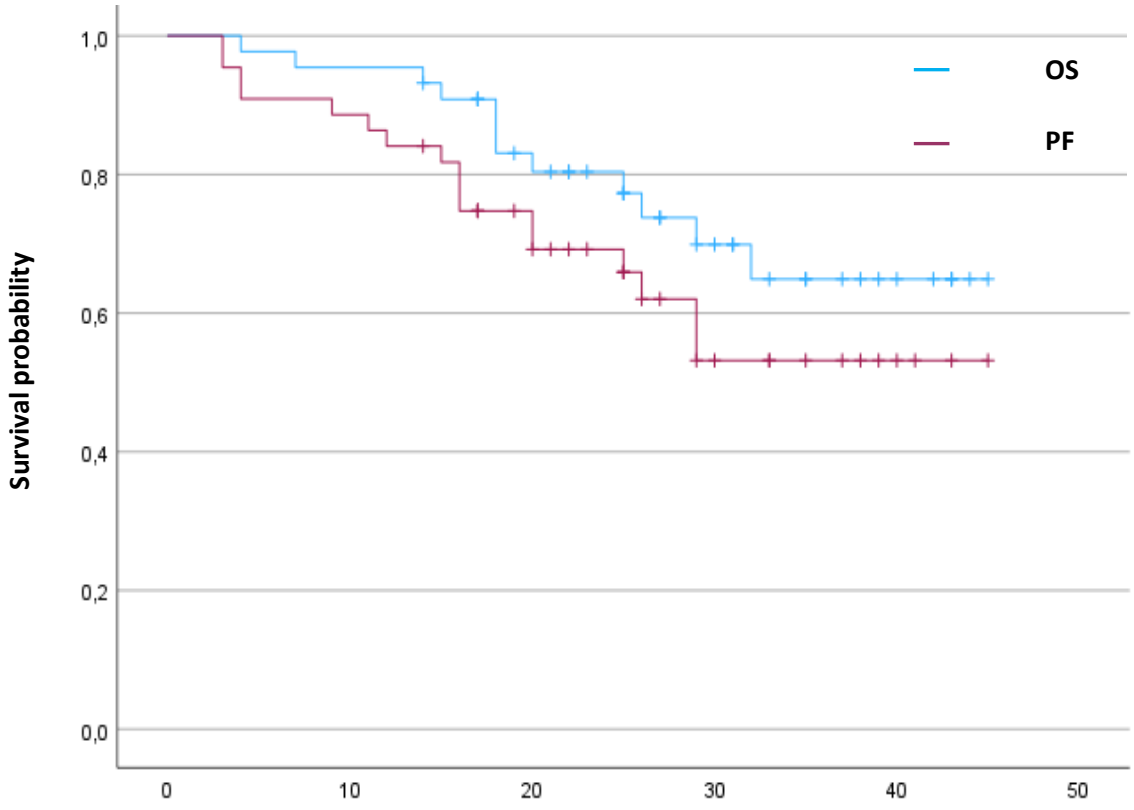
1A



1B



1C



Supplemental Figure 1 Hematologic Response Rates under Venetoclax
1A Response rates for the whole cohort at baseline and after 3, 6, 12, 24 and 36 months repectively. Time to best response was 3 months and best response (including CR and VGPR) could be maintained long-term. Corticosteroids were given in a subset off patientes to enhance treatment response or to alleviate side effects. **1B Best hematologic response** in all evaluable patients (n=44). **Fig. 1C Kaplan-Meier Curves** for event free survival (EFS, purple) and overall survival (blue), mEFS and mOS was not reached.

SUPPLEMENTAL TABLE 1:
Patient demographics and characteristics (%), n = 44

Age (Median, range)		68, 45-78
Male		24 (55)
Lambda restricted		30 (68)
Paraproteinemia	MG	11 (25)
	Smoldering M	30 (68)
	MM	2 (5)
	M. W.	1 (2)
t(11;14)		42 (95) (1 MW, 1 n.a.)
iFISH test results UKHD		33 (75)
atypical t(11;14)		12 (36)
typical t(11;14)		21 (64)
amplification of 1q21		5 (11)
dFLC at initiation in mg/l (median, range)		91 (0-1,178)
dFLC over 180 mg/dl		7 (16)
Organ involvement:	Heart	39 (89)
	Renal	32 (73)
	Liver	10 (23)
	Other	26 (59)
More >/= 2 organs involved		37 (84)
NTproBNP at baseline (pg/ml) **(median, range)**		2755 (247-57,000)
Median eGFR at baseline (ml/min) **(median, range)**		44 (6-109)
Median Proteinuria at baseline (g/d) **(median, range)**		3,0 (0.1-26)
Median AP at baseline (U/l) **(median, range)**		101 (88-1,084)
>/ one line of prior therapy		39 (89)
Median		3
Previous therapy lines including:		
	Daratumumab	42 (95)
	refractory	37 (84)
	Bortezomib	38 (86)
	Cyclophosphamide	15 (34)
	Lenalidomide	24 (55)
	Pomalidomide	11 (25)
	Melphalan	19 (43)
	ABSCT	

heart transplant	7 (15)
other:	1 (2) 3 (7)
Reasons to start Venetoclax	
Refractory disease Relapse Non-optimal hematological response	15 (34) 10 (23) 19 (43)
Hematologic response at baseline	
CR (MRD positive in bone marrow)	1 (2)
VGPR	12 (27)
PR	10 (23)
non-response	7 (16)
PD	14 (32)

Supplemental Table 1: Categorical data are shown as counts (% of respective total), continuous data are shown as medians (range). MG: monoclonal gammopathy. Smoldering M: smoldering myeloma. MM: multiple myeloma. M. W.: Morbus Waldenstrom`s disease. dFLC: difference between involved and uninvolved free light chains. NTproBNP: N-terminal Pro-B-type natriuretic peptide. eGFR: estimated glomerular filtration rate. AP: alkaline phosphatase. ASCT: autologous stem cell transplantation. CTC: common toxicity criteria. ORR: overall response rate. mDOR: median duration of response. mEFS: median event free survival.

SUPPLEMENTAL TABLE 2:
Response rates and toxicities

Dosis in mg/day	50 - 400
Best hematological response	
CR	17 (39)
VGPR	17 (39)
PR	7 (16)
SD	1 (2)
PD	2 (5)
Time to best hematological response (median in months)	3
PD	11 (25)
Median time to PD in months, range	17, 0-24
Primarily refractory	2 (4)
Ongoing response under Venetoclax	48 (21)
Ongoing response, Venetoclax off	1 (5)
Organ response after 12 months	
Cardiac **34 evaluable after 3, 6, or 12 months (92%)***	9 (39)
Renal **22 evaluable after 3, 6, or 12 months (69%)***	10 (62)
Liver **10 evaluable after 3, 6, or 12 months (100%)***	3 (37)
Addition of Dexamethason	12 (27)
Dose of dexamethason in mg	
- 12 mg	6 (50)
- 8 mg	5 (42)
- 4 mg	1 (8)
Months until Start Dex	
- Upfront	3 (25)
- Within 6 months	5 (42)
- After 12 months	2 (17)
- After 18 months	2 (17)
ORR	41 (93)
ORR (VGPR&CR)	34 (77)
Time to best response in months	7
mDOR in months	21
mEFS in months	32
mOS in month	37

mEFS in months	32
mOS in months	36
12 months EFS in %	86
12 months OS in %	95

Infections	Hematological Toxicities	GI	Dose Reduction	Treatment discontinuation	Death on therapy
5 (11) **CTC Grade 3: II (both pulmonary)**	8 (18) CTC grade 4: I (Neutropenia) CTC grade 3: I (low platelets)	8 (18)	29 (66)	19 (43) 2: toxicity, ongoing hematologic response 2: CR/VGPR, ongoing response 11: PD, 6 with dose reduction due to toxicity before 2: renal organ progress 2: new oncological diagnoses (new MM clone, newly diagnosed ovarian carcinoma)	6 (14): 1: suicide 1: intestinal ischemia 4: Organ complication of AL

SUPPELEMTAL TABLE 2: Categorical data are shown as counts (% of respective total). *For organ response rates after 12 months % is calculated for the respective organs involved. ORR: overral response rate. mDOR: median duration of repsonse. mEFS: median event free survival; mOS: median overall survival. CTC: common toxicity criteria.