### Supplementary information

- 2 The supplementary information includes five supplementary tables and one supplementary figure.
- 3 Table S1. Adverse events not considered in the manuscript that occurred prior to cut-off but were reported after the data
- 4 analysis snapshot

AE	Age, years (gender)	Onset (study day)	End (study day)	Grade	SAE	Relationship to obinutuzumab/ chemotherapy	Outcome
Hepatitis E	58 (F)	570	1024	3	Υ	Related to obinutuzumab and chemotherapy	Resolved
Neutropenia	66 (M)	113	NA	2	N	Related to chemotherapy	Ongoing
Myelosuppression	61 (M)	181	203	3	N	Related to chemotherapy	Resolved
Headache	41 (M)	NA	755	3	Υ	Not related	Resolved with sequelae
Fatigue*	58 (F)	161	NA	1	N	Related to obinutuzumab and chemotherapy	Ongoing
Neuropathy*	58 (F)	245	480	1	N	Related to obinutuzumab and chemotherapy	Resolved
Febrile neutropenia	50 (M)	99	99	3	Υ	Related to obinutuzumab and chemotherapy	Resolved

<sup>\*</sup>AEs occurred in the same patient. AE, adverse event; F, female; M, male; N, no; NA, not available; SAE, serious adverse event; Y, yes.

## **Table S2.** Change in final response assessment\*

7

	Age, years (gender)	Primary analysis snapshot	Updated to
Response	58 (M)	CR	CRi

<sup>\*</sup>After the data analysis snapshot was taken, one response was changed from CR to CRi by a site on the database that remained open to continue collecting information until the final analysis.

<sup>10</sup> CR, complete response; CRi, complete response with incomplete marrow recovery; M, male.

	N (%) of patients reporting IRRs ( $N = 140$ )
Any IRR	97 (69.3)
Grade ≥3 IRRs	27 (19.3)
Serious IRRs	13 (9.3)
IRRs leading to treatment discontinuation	1 (<1.0)
IRRs (reported by ≥2% patients, any grade by preferred term)	
Pyrexia	27 (19.3)
Nausea	21 (15.0)
Chills	11 (7.9)
Vomiting	10 (7.1)
Dyspnea	10 (7.1)
Rash	9 (6.4)
Hypertension	8 (5.7)
Hyperhidrosis	7 (5.0)
Chest discomfort	7 (5.0)
Hyperthermia	7 (5.0)
Hypotension	7 (5.0)
Headache	6 (4.3)
Thrombocytopenia	6 (4.3)
Alanine aminotransferase increased	5 (3.6)
Aspartate aminotransferase increased	5 (3.6)
Hot flush	5 (3.6)
Cytokine release syndrome	4 (2.9)
Tachycardia	4 (2.9)
Asthenia	3 (2.1)
Anemia	3 (2.1)

Neutropenia	3 (2.1)
Tumor lysis syndrome	3 (2.1)

13 IRRs, infusion-related reactions.

15 **Table S4.** Listing of grade 5 (fatal) adverse events (safety population)

AE (preferred term)	Age, years (gender)	Treatment period (onset of event)*	AESI	AEPI	Relationship to obinutuzumab/ chemotherapy
Unexplained death	65 (M)	Post (Day 146)	N	N	Not related
Sepsis	74 (F)	Post (Day 180)	Υ	N	Not related
Acute fibrinous organizing pneumonia	47 (F)	During (Day 105)	N	N	Related to obinutuzumab and chemotherapy
Acute myeloid leukemia	64 (M)	Post (Day 903)	N	Υ	Not related

<sup>\*</sup>Post = post treatment period; during = during treatment period.

AE, adverse event; AEPI, adverse events of particular interest; AESI, adverse event of special interest; F, female; M, male; N, no; Y, yes.

Table S5. Minimal residual disease response in peripheral blood and bone marrow according

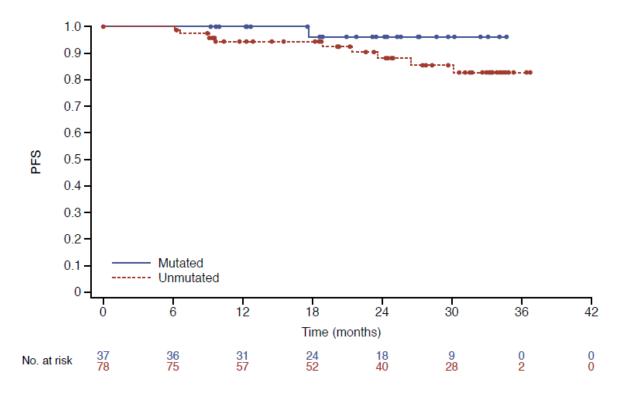
## 19 to IGHV mutation status

n/N (%)	All patients (N = 140)		
Peripheral blood			
IGHV mutated	N = 37		
Number of patients included in analysis	29		
MRD negative	28/29 (96.6)		
MRD positive	0		
MRD unknown	1/29 (3.4)		
IGHV unmutated	N = 77		
Number of patients included in analysis	59		
MRD negative	54/59 (91.5)		
MRD positive	5/59 (8.5)		
Bone marrow			
IGHV mutated	N = 37		
Number of patients included in analysis	21		
MRD negative	14/21 (66.7)		
MRD positive	7/21 (33.3)		
IGHV unmutated	N = 77		
Number of patients included in analysis	43		
MRD negative	31/43 (72.1)		
MRD positive	11/43 (25.6)		
MRD unknown	1 (2.3)		

IGHV, immunoglobulin heavy chain variable region; MRD, minimal residual disease.

# Fig. S1. Kaplan-Meier plot of progression-free survival according to IGHV mutation status

## (ITT population)



IGHV, immunoglobulin heavy chain variable region; ITT, intent-to-treat; PFS, progression-free survival.