UNIKLINIK KÖLN | Department I of Internal Medicine University Hospital of Cologne

DEUTSCHE CLL STUDIENGRUPPE

S146 I VENETOCLAX-OBINUTUZUMAB FOR PREVIOUSLY UNTREATED CHRONIC LYMPHOCYTIC LEUKEMIA: FINAL ANALYSIS OF THE RANDOMIZED PHASE 3 CLL14 STUDY

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EHA**2026** | Congress | June 11-14 | Stockholm, Sweden

/01 RATIONALE

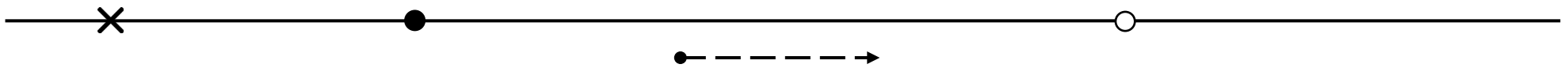
CLL14

TO STUDY THE EFFICACY AND SAFETY OF **FIXED-DURATION VENETOCLAX-OBINUTUZUMAB** IN COMPARISON TO FIXED-DURATION CHLORAMBUCIL-OBINUTUZUMAB IN PATIENTS WITH PREVIOUSLY UNTREATED CHRONIC LYMPHOCYTIC LEUKEMIA.

CLL14 is a collaborative effort of the German CLL Study Group, F. Hoffmann-La Roche Ltd. and AbbVie Inc.

/02 CONTEXT

Venetoclax Development



CONTINUOUS MONOTHERAPY

FIXED-DURATION COMBINATION THERAPY

THERAPY-FREE INTERVAL

RE-TREATMENT

Seymour J et al., *New Engl. J. Med. 2018*
Fischer K et al., *New Engl. J. Med. 2019*

/03 PROFILE

CLL14

POPULATION	Previously Untreated Patients with CLL And With Coexisting Medical Conditions (CIRS > 6 and/or CrCl < 70ml/min)
TREATMENT	Venetoclax–Obinutuzumab 6 Cycles Plus Venetoclax 6 Cycles Or Chlorambucil–Obinutuzumab 6 Cycles Plus Chlorambucil 6 Cycles
ENDPOINTS	Primary Endpoint: Progression-Free Survival, Key Secondary Endpoints: Time-To-Next Treatment, Overall Survival, Minimal Residual Disease, Safety
SITES	Conducted in 21 Countries at 196 Sites
SAFETY RUN-IN	December 2014 – April 2015
RECRUITMENT	August 2015 – August 2016
FIRST DATA CUT-OFF	August 2018
LAST DATA CUT-OFF	October 2025

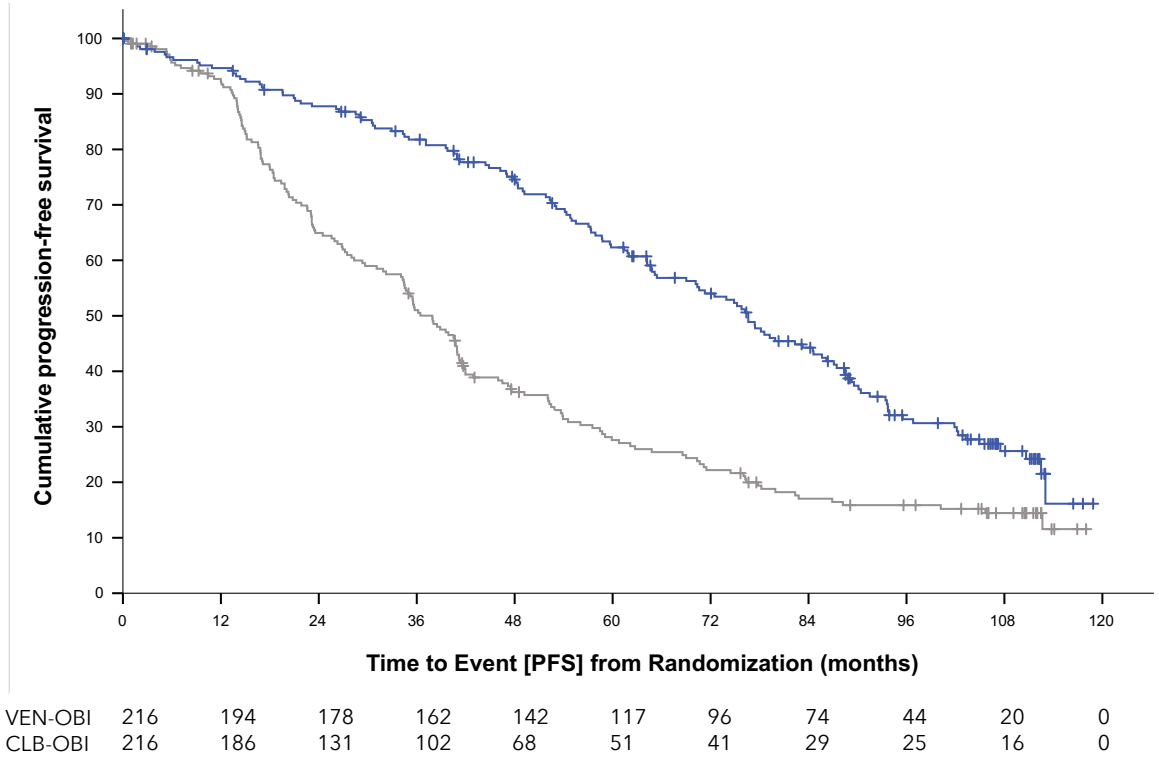
Fischer K et al., *Blood 2017*
Fischer K et al., *New Engl. J. Med. 2019*
Al-Sawaf O et al., *Lancet Oncol. 2020*
Al-Sawaf O et al., *JCO 2021*
Al-Sawaf O et al., *Nat. Commun. 2023*
Al-Sawaf O et al., *Blood 2024*

CLL14

TREATMENT	VEN-OBI (N=216)	CLB-OBI (N=216)
MEDIAN AGE	72 years	71 years
MEDIAN CIRS SCORE	9	8
MEDIAN CREATININE CLEARANCE	65.2 ml/min	67.4 ml/min
IGHV UNMUTATED	61%	60%
TP53 DELETED AND/OR MUTATED	12%	11%

/05 KAPLAN-MEIER ESTIMATES

Progression-Free Survival

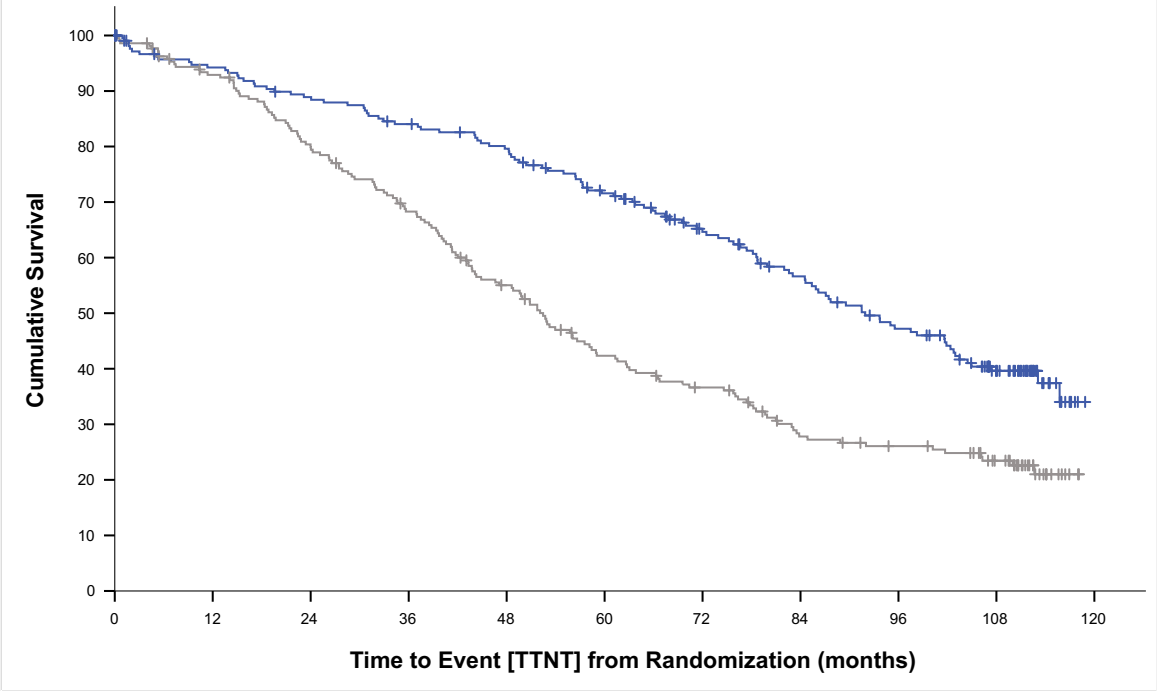


MEDIAN OBSERVATION TIME	110.1 months
MEDIAN PFS VEN-OBI	76.6 months
9-YEAR PFS VEN-OBI	25.6%
MEDIAN PFS CLB-OBI	37.9 months
9-YEAR PFS CLB-OBI	14.4%
HAZARD RATIO	0.50, 95% CI 0.39-0.63
P VALUE	<0.001

MEDIAN PFS FOR VEN-OBI
6.4 YEARS

/05 KAPLAN-MEIER ESTIMATES

Time-To-Next Treatment

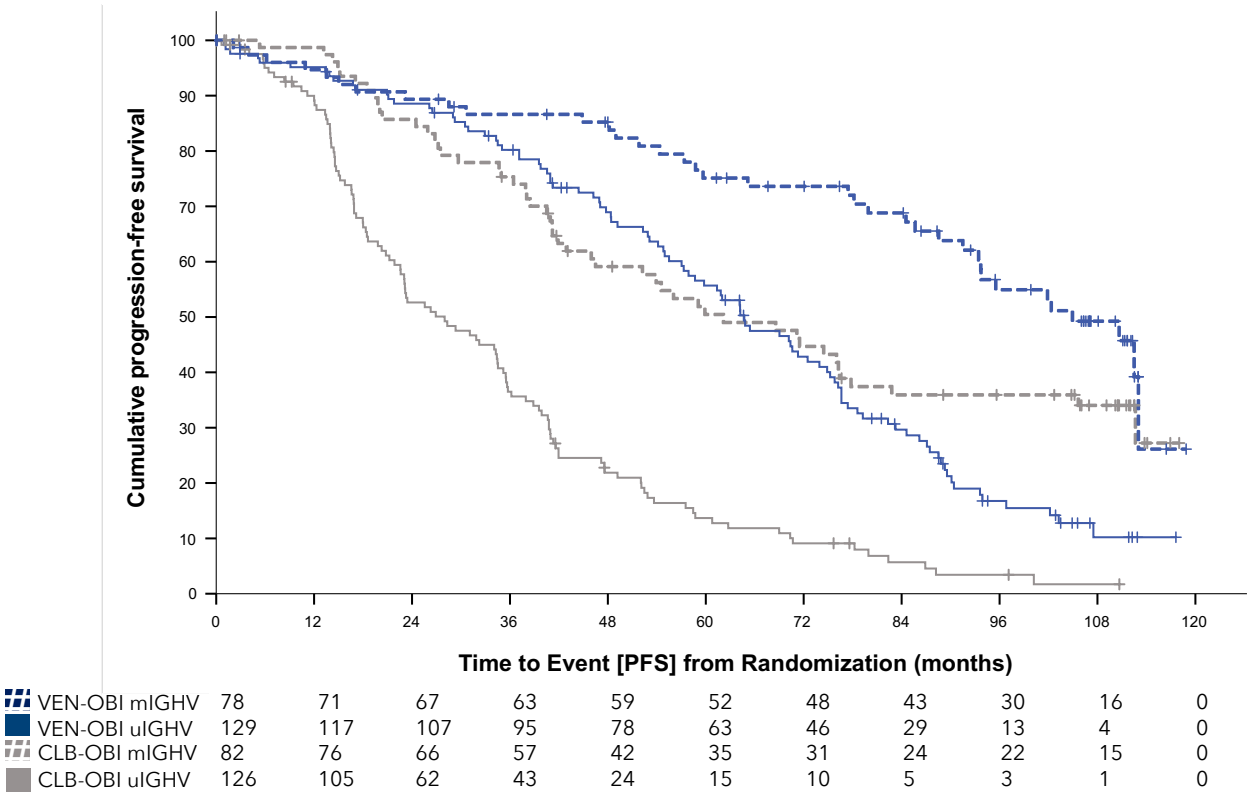


MEDIAN OBSERVATION TIME	110.1 months
MEDIAN TTNT VEN-OBI	91.9 months
9-YEAR TTNT VEN-OBI	39.6%
MEDIAN TTNT CLB-OBI	52.5 months
9-YEAR PFS CLB-OBI	23.5%
HAZARD RATIO	0.54, 95% CI 0.43-0.70
P VALUE	<0.0001
NEXT ANTI-LEUKEMIC THERAPY	
VEN-OBI	87 PDs – 54 NALT
CLB-OBI	144 PDS – 111 NALT

MEDIAN TTNT FOR VEN-OBI
7.7 YEARS

/05 KAPLAN-MEIER ESTIMATES

Progression-Free Survival By IGHV Mutational Status

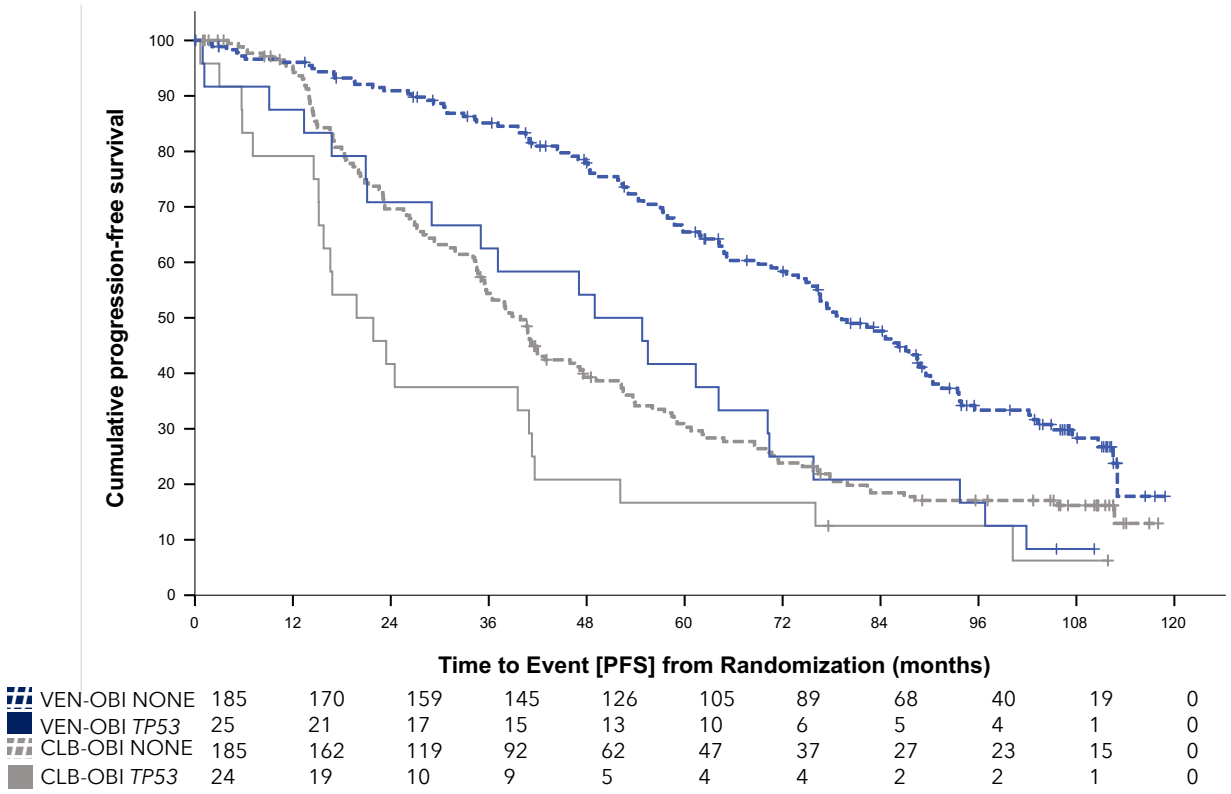


MEDIAN OBSERVATION TIME	110.1 months
MEDIAN PFS VEN-OBI & mIGHV	104.9 months
MEDIAN PFS VEN-OBI & uIGHV	64.7 months
HAZARD RATIO	2.74, 95% CI 1.85-4.06
P VALUE	<0.001
MEDIAN PFS CLB-OBI & mIGHV	62.2 months
MEDIAN PFS CLB-OBI & uIGHV	28.0 months
HAZARD RATIO	3.13, 95% CI 2.21-4.45
P VALUE	<0.001

MEDIAN PFS VEN-OBI mIGHV 8.7 YEARS
MEDIAN PFS VEN-OBI uIGHV 5.4 YEARS

/05 KAPLAN-MEIER ESTIMATES

Progression-Free Survival By *TP53* Del/Mut

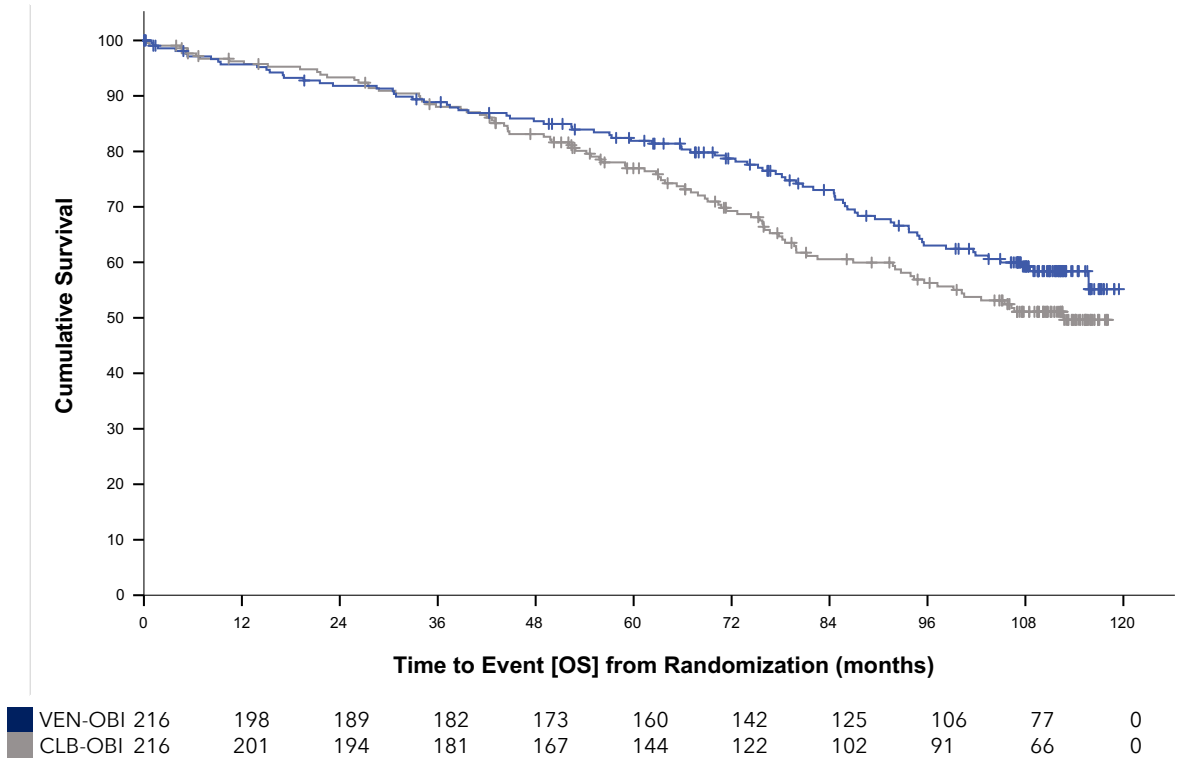


MEDIAN OBSERVATION TIME	110.1 months
MEDIAN PFS VEN-OBI & NONE	79.2 months
MEDIAN PFS VEN-OBI & *TP53*	49.0 months
HAZARD RATIO	2.15, 95% CI 1.36-3.40
P VALUE	=0.001
MEDIAN PFS CLB-OBI & NONE	39.9 months
MEDIAN PFS CLB-OBI & *TP53*	19.8 months
HAZARD RATIO	1.68, 95% CI 1.07-2.64
P VALUE	=0.024

MEDIAN PFS FOR VEN-OBI *TP53*
4.1 YEARS

/05 KAPLAN-MEIER ESTIMATES

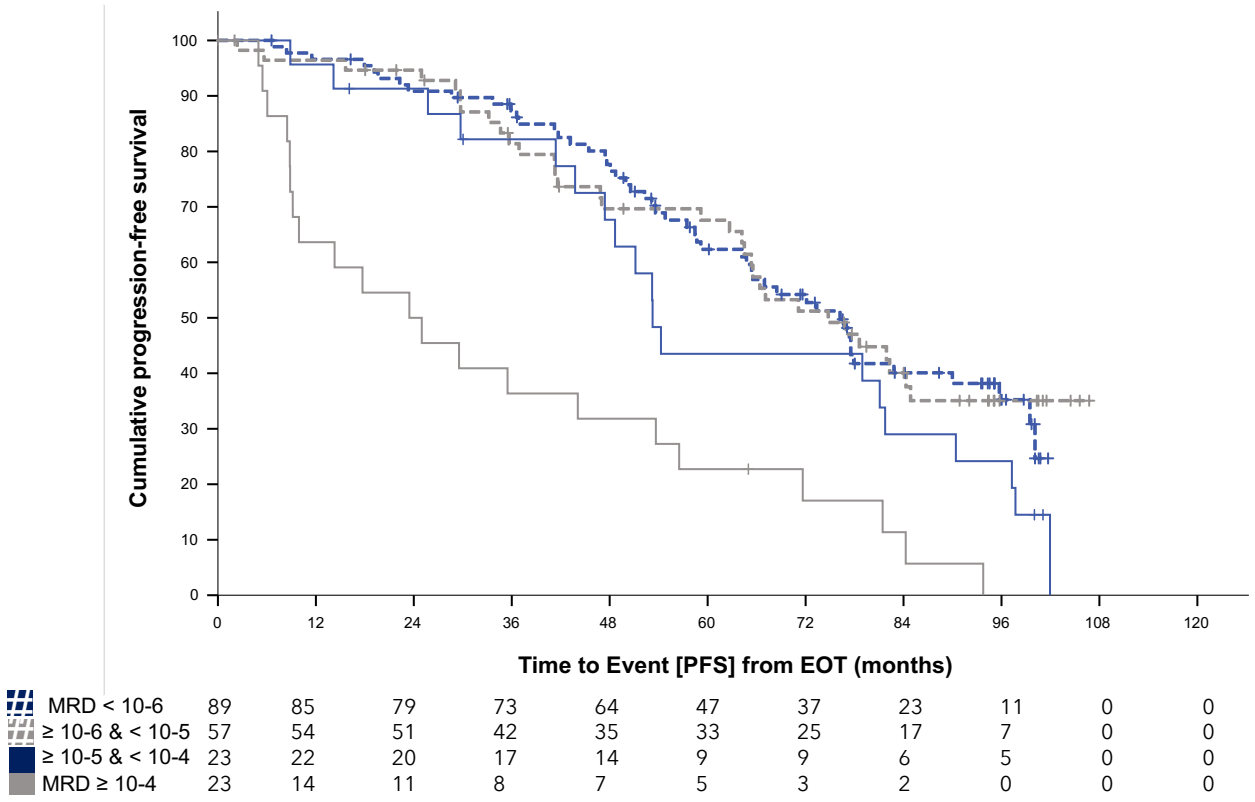
Overall Survival



MEDIAN OBSERVATION TIME	110.1 months
MEDIAN OS VEN-OBI	Not reached
9-YEAR OS VEN-OBI	59.3%
MEDIAN OS CLB-OBI	112.7 months
9-YEAR OS CLB-OBI	51.1%
HAZARD RATIO	HR 0.8, 95% CI 0.59-1.09
P VALUE	=0.161
CAUSES OF DEATH	VEN-OBI vs CLB-OBI
INFECTION	22 versus 21
PROGRESS/RT	**14 versus 30**
SPM	10 versus 10
OTHER	32 versus 31

MEDIAN OS FOR VEN-OBI
NOT REACHED

Progression-Free Survival & MRD Status For Ven-Obi



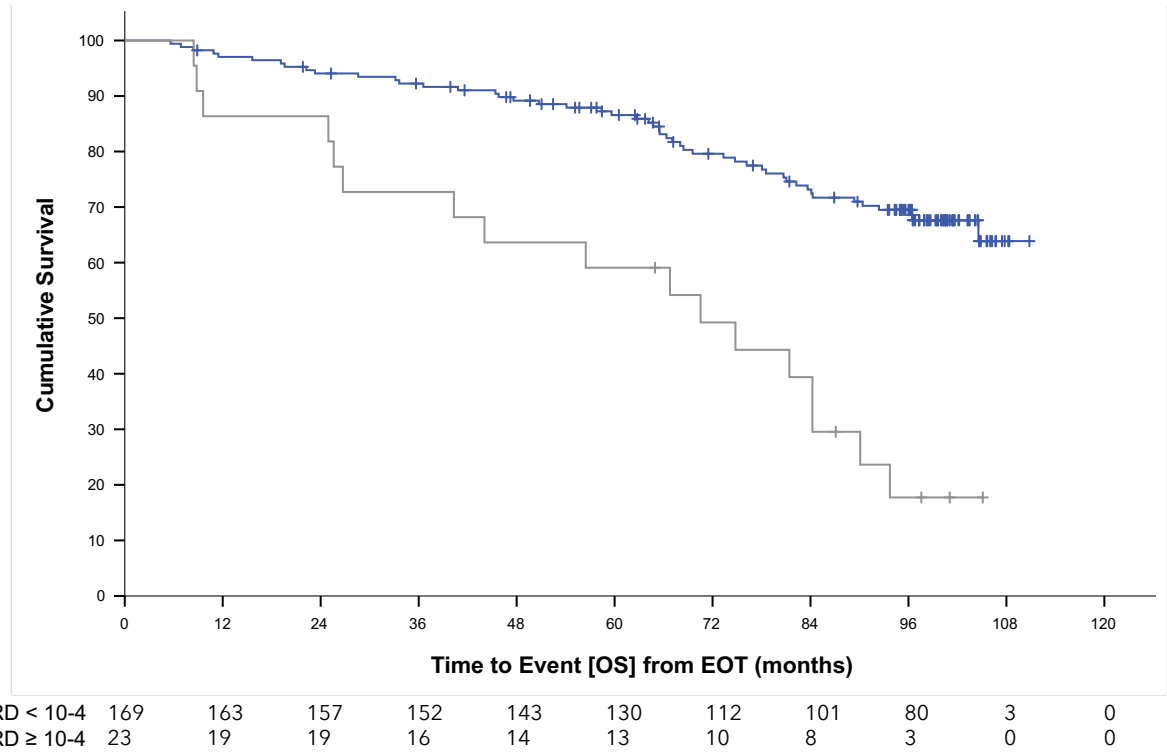
MEDIAN OBSERVATION TIME	110.1 months
MRD < 10^{-6}	76.2 months
MRD ≥ 10^{-6} and< 10^{-5}	74.8 months
MRD ≥ 10^{-5} and < 10^{-4}	53.3 months
MRD ≥ 10^{-4}	23.5 months

MRD STATUS AFTER VEN-OBI REMAINS PROGNOSTIC FOR PFS

MRD MEASURED IN PERIPHERAL BLOOD BY NGS AT THE END OF TREATMENT

/06 LANDMARK ANALYSIS

Overall Survival & MRD Status For Ven-Obi



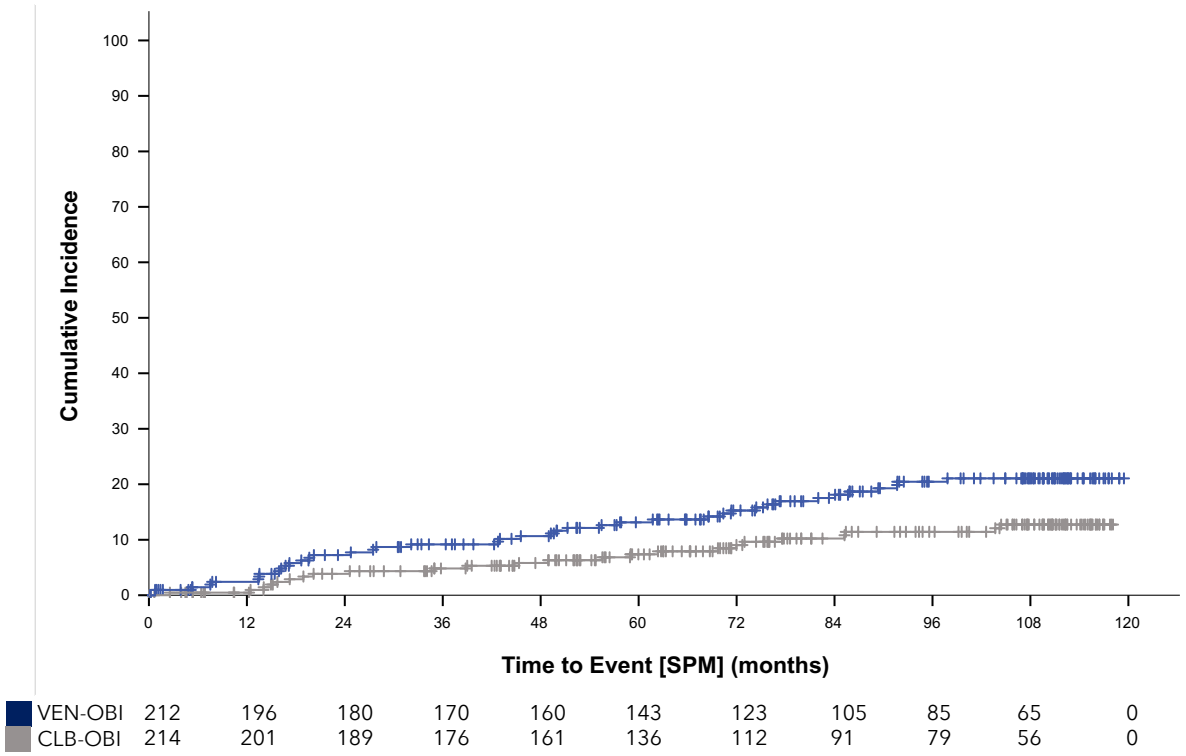
MEDIAN OBSERVATION TIME	110.1 months
MRD < 10-4	Not reached
MRD ≥ 10-4	70.5 months
HAZARD RATIO	3.73, 95% CI 2.14-6.50

MRD STATUS AFTER VEN-OBI REMAINS PROGNOSTIC FOR OS

MRD MEASURED IN PERIPHERAL BLOOD BY NGS AT THE END OF TREATMENT

/07 CUMULATIVE AND FOLLOW-UP ADJUSTED INCIDENCE

Second Primary Malignancies



MEDIAN OBSERVATION TIME	110.1 months
FOLLOW-UP ADJUSTED INCIDENCE RATE PER 1000 PATIENT MONTHS	
VEN-OBI (212 PATIENTS)	2.6
CLB-OBI (214 PATIENTS)	1.5
P VALUE	=0.047
TYPE OF SPM	VEN-OBI vs CLB-OBI
SOLID	27 versus 18
MELANOMA	9 versus 4
HEMATOLOGICAL	4 versus 3
OTHER	2 versus 1

HIGHER INCIDENCE OF SPM IN VEN-OBI GROUP THAN IN CLB-OBI GROUP

/08 SUMMARY

Venetoclax-Obinutuzumab

1	MEDIAN PROGRESSION-FREE SURVIVAL (PFS) OF APPROXIMATELY 6 YEARS
2	MEDIAN TIME-TO-NEXT TREATMENT OF APPROXIMATELY 8 YEARS
3	MEDIAN OVERALL SURVIVAL (OS) NOT REACHED
4	END-OF-TREATMENT MRD STATUS REMAINS STRONG PROGNOSTIC FACTOR FOR PFS AND OS
5	INCIDENCE OF SPM INCREASED COMPARED TO CHLORAMBUCIL-OBINUTUZUMAB

Venetoclax-Obinutuzumab

THE FINAL 9-YEAR RESULTS OF CLL14 CONFIRM THAT **ONE YEAR FIXED-DURATION VENETOCLAX-OBINUTUZUMAB ACHIEVES ENDURING LONG-TERM EFFICACY** IN PREVIOUSLY UNTREATED PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA

ADDRESSING THE QUESTIONS WE KEEP ASKING

1	OBSERVATION OF A PRE-DEFINED PATIENT POPULATION
2	CLL13. CLL14. CLL17.
3	MAJORITY OF PATIENTS - APPROXIMATELY 2000 - REMAIN ALIVE AT TRIAL CLOSURE
4	DATA COMES FROM ANNUAL CLINICAL ROUTINE VISIT
5	SURVIVAL STATUS. DISEASE STATUS. SUBSEQUENT THERAPY. SPM. RT. QOL.
6	OPTIONAL BLOOD SAMPLING
7	NO INTERVENTION. NO MONITORING. EASY DOCUMENTATION.
8	LOW EFFORT. BIG IMPACT. LET´S CONNECT!