# CLL: News from the EHA Congress 2020

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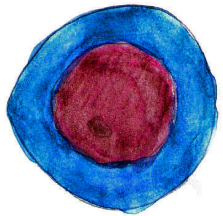


DEUTSCHE STUDIENGRUPPE

CECAD COLOGNE Excellent in Aging Research – Exzellent in Alternsforschung

CIO Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf

# Disclosure

- Research support: Roche, Gilead, Mundipharma, Janssen, Celgene, Pharmacyclics, Abbvie

- Honoraria (speaker's bureau and/or advisory board): Roche, Gilead, Mundipharma, Janssen, Celgene, Pharmacyclics, Abbvie

EUROPEAN HEMATOLOGY ASSOCIATION
EHA25 VIRTUAL

Abstract S155

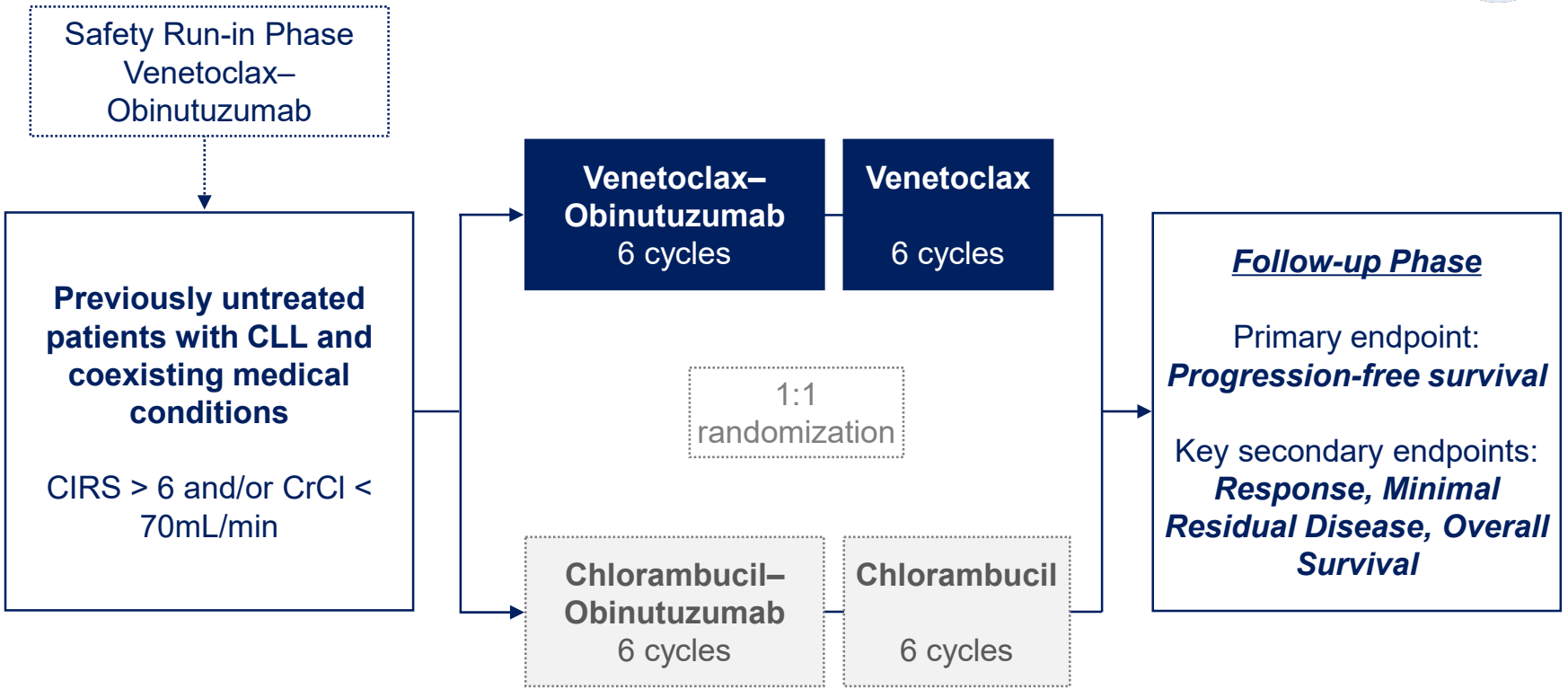
# FIXED-DURATION **VENETOCLAX-OBINUTUZUMAB** FOR PREVIOUSLY UNTREATED **CHRONIC LYMPHOCYTIC LEUKAEMIA**: FOLLOW-UP OF EFFICACY AND SAFETY RESULTS FROM THE MULTICENTER, OPEN-LABEL, RANDOMIZED PHASE 3 **CLL14 TRIAL**

**Othman Al-Sawaf**, Can Zhang, Maneesh Tandon, Arijit Sinha, Anna-Maria Fink, Sandra Robrecht, Olga Samoylova, Anna Marina Liberati, Javier Pinilla-Ibarz, Stephen Opat, Liliya Sivcheva, Katell Le Dû, Laura Maria Fogliatto, Carsten Utoft Niemann, Robert Weinkove, Sue Robinson, Thomas J Kipps, Eugen Tausch, William Schary, Matthias Ritgen, Clemens-Martin Wendtner, Karl-Anton Kreuzer, Barbara Eichhorst, Stephan Stilgenbauer, Michael Hallek, and Kirsten Fischer

12th June 2020
CLL - Targeted therapy I

CLL-14
DEUTSCHE STUDIENGRUPPE CLL

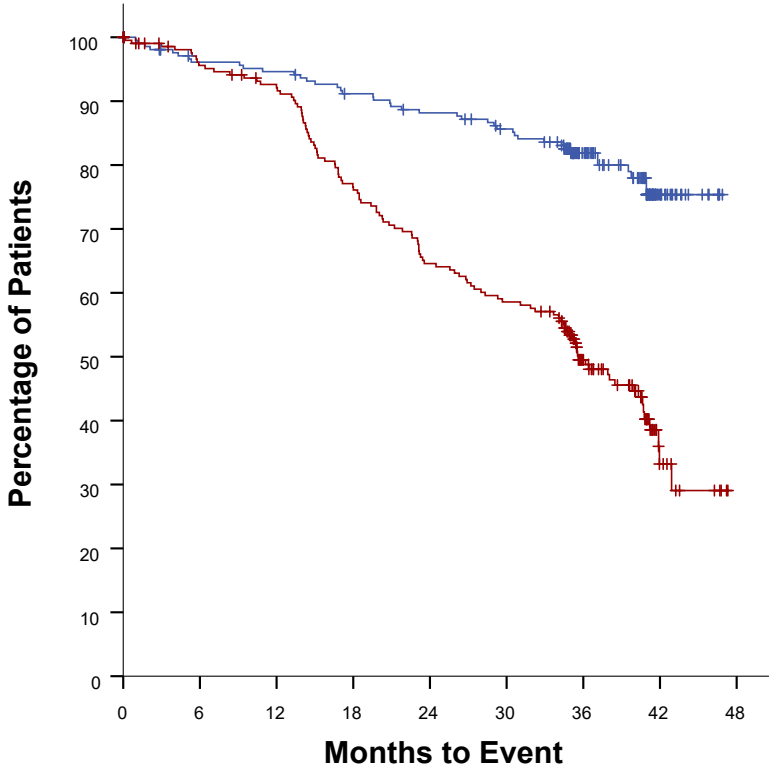
# TRIAL DESIGN




Fischer et al, New Engl J Med 2019

# PROGRESSION-FREE SURVIVAL

Median observation time 39.6 months




**Median PFS**

Ven-Obi: not reached

Clb-Obi: 35.6 months

**3-year PFS rate**

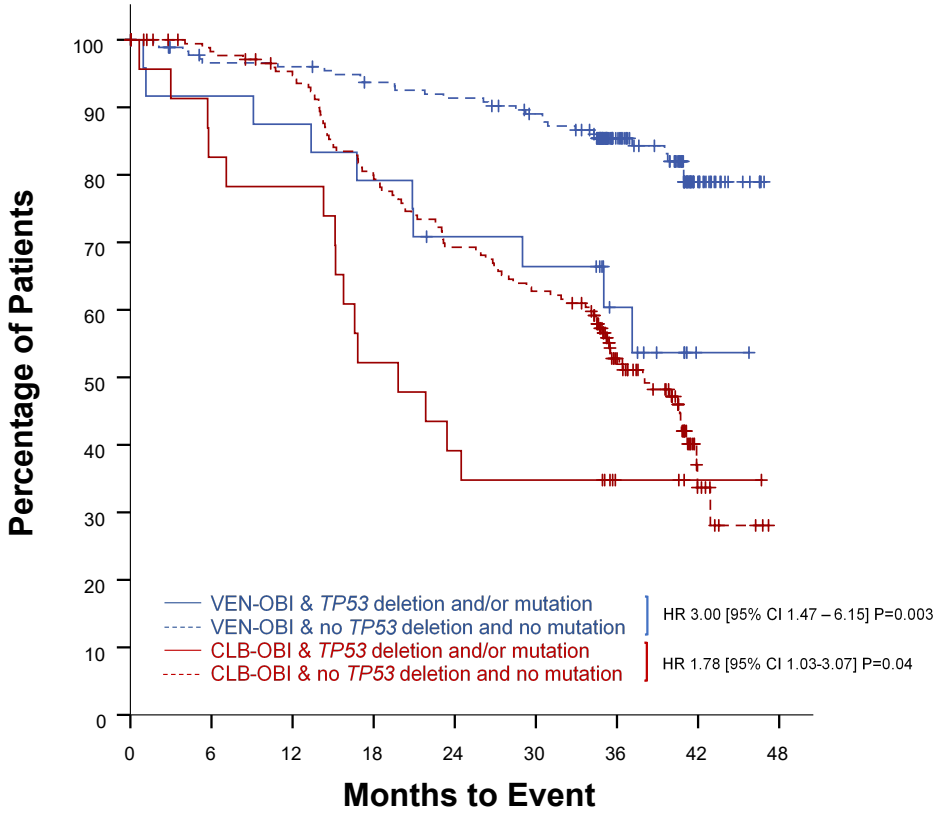
Ven-Obi: 81.9%

Clb-Obi:49.5%

HR 0.31, 95% CI [0.22-0.44], P<0.0001

# PROGRESSION-FREE SURVIVAL

According to *TP53*del/mut status




**Median PFS**

Ven-Obi without TP53del/mut: not reached

Ven-Obi with TP53del/mut: not reached

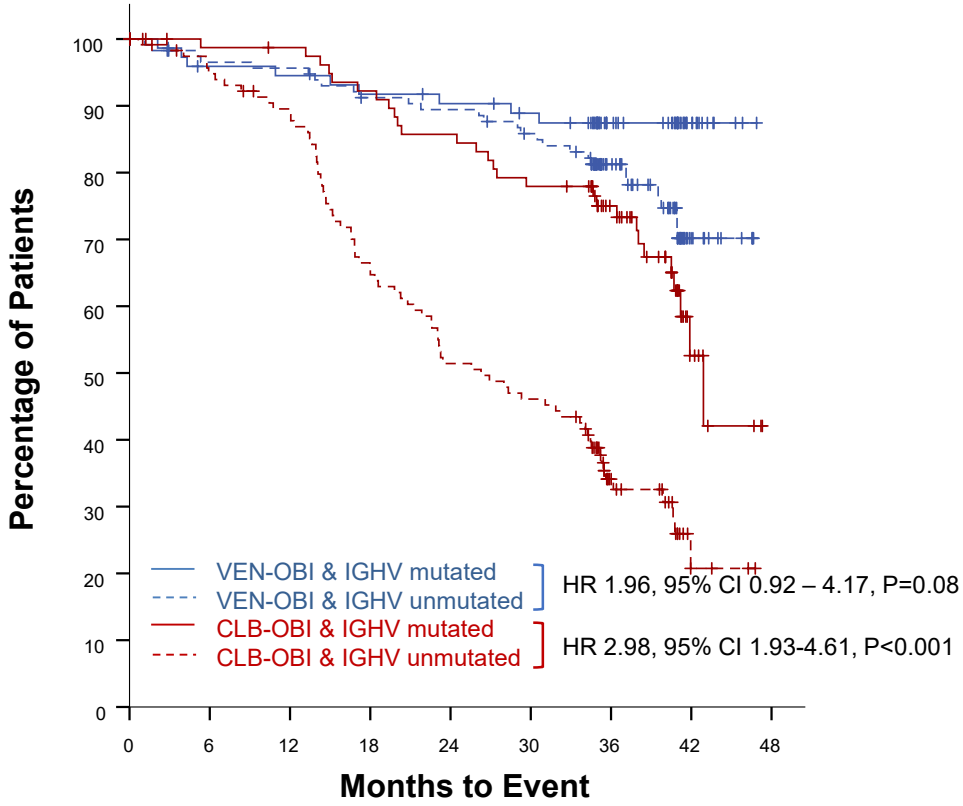
**3-year PFS rate**

Clb-Obi without TP53del/mut : 19.8 months

Clb-Obi with TP53del/mut : 38.0 months

# PROGRESSION-FREE SURVIVAL

According to *IGHV* status




**Median PFS**

Ven-Obi IGHV*mut*: not reached

Ven-Obi IGHV*unmut*: not reached

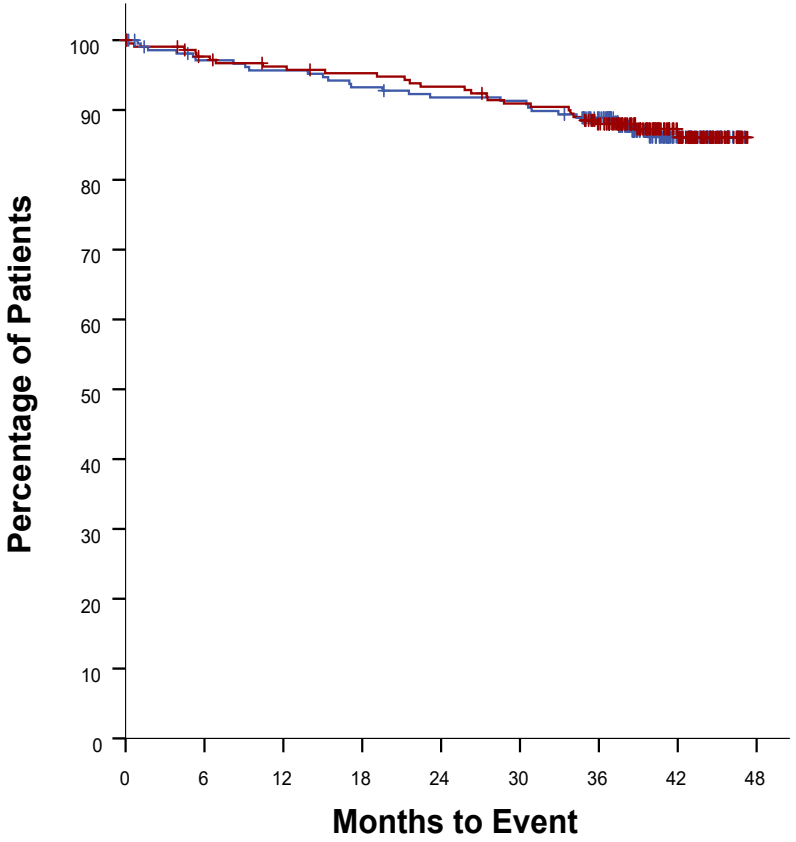
**3-year PFS rate**

Clb-Obi IGHV*mut*: 42.9 months

Clb-Obi IGHV*unmut*: 26.3 months

# OVERALL SURVIVAL

Median observation time 39.6 months




**Median OS**

Ven-Obi: not reached

Clb-Obi: not reached

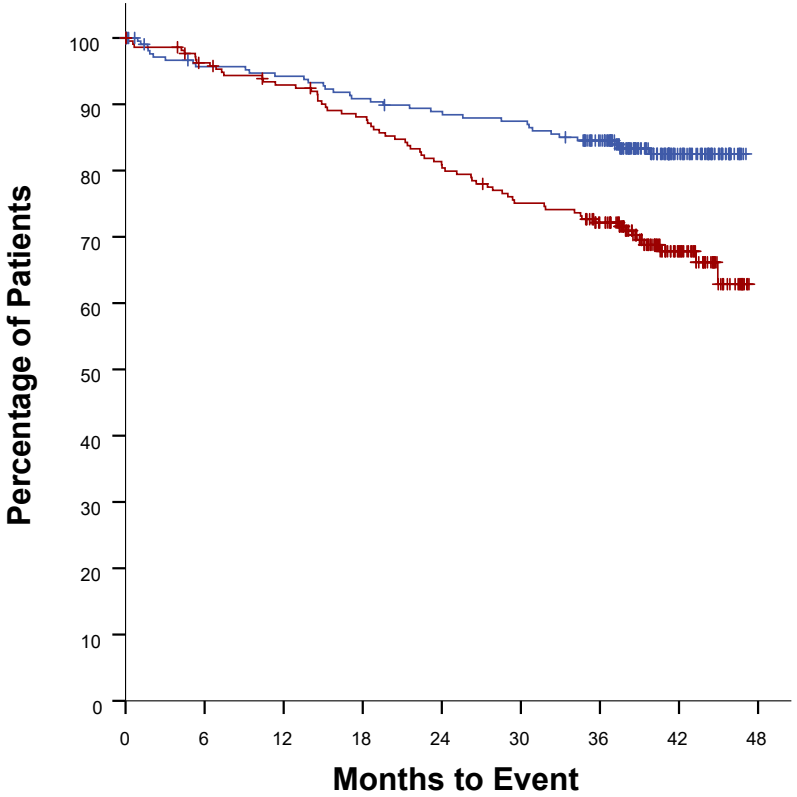
**3-year OS rate**

Ven-Obi: 89.9%

Clb-Obi: 88.0%

HR 1.027, 95% CI [0.60-1.75], P=0.0921

# TIME TO NEXT TREATMENT




**Median TTNT**
Ven-Obi: not reached
Clb-Obi: not reached

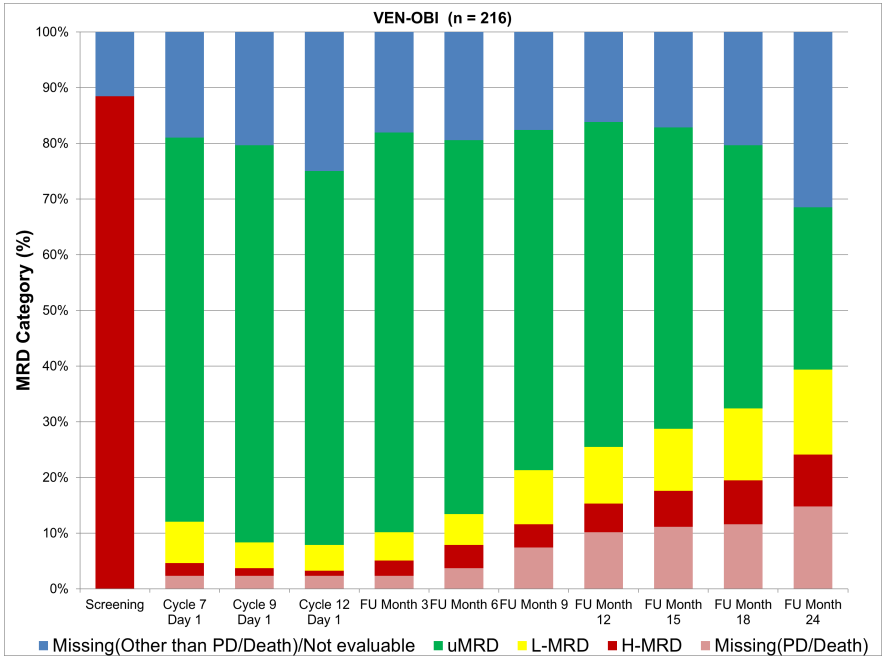
**3-year TTNT rate**
Ven-Obi: 84.5%
Clb-Obi: 72.1%

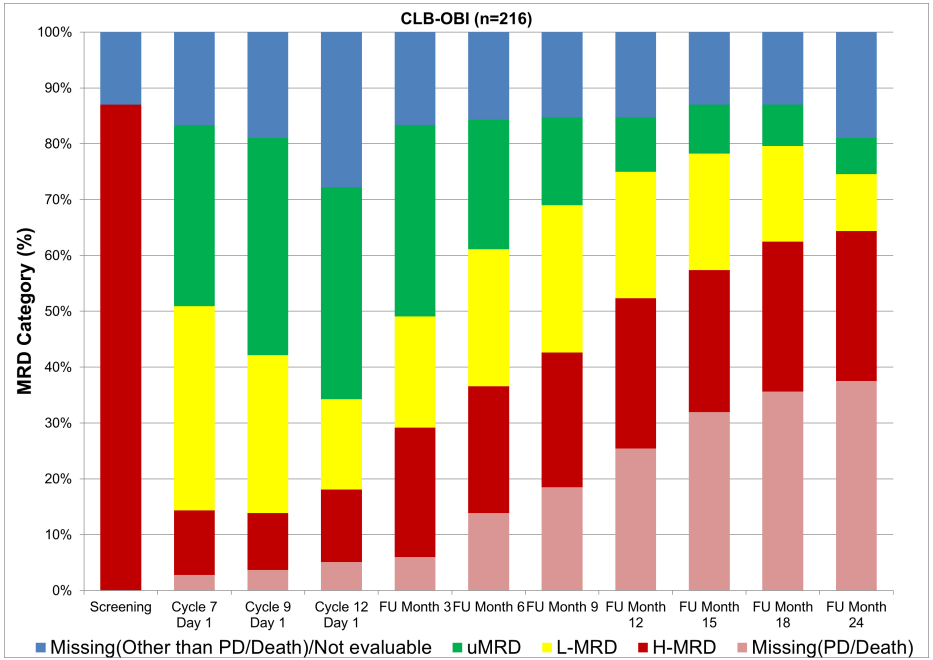
HR 0.51, 95% CI [0.341-.0775]

**Next anti-leukemic therapy:**
Ven-Obi: 21 PDs – 9 NLT
Clb-Obi: 102 – 44 NLT

# MRD KINETICS

By ASO-PCR in peripheral blood




**uMRD rate at 18month FU**

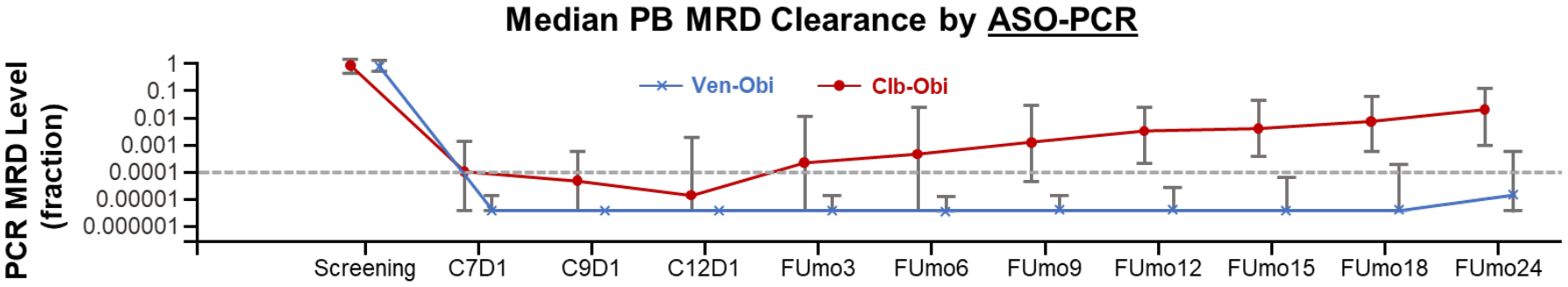
Ven-Obi: 47.2%

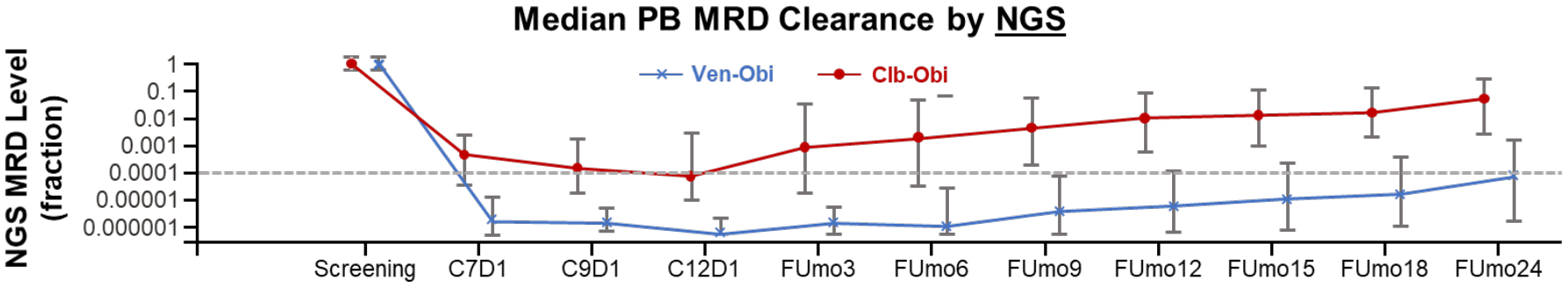
Clb-Obi: 7.4%

- uMRD $<10^{-4}$
- L-MRD $10^{-4} < 10^{-2}$
- H-MRD $\geq 10^{-2}$

# MRD KINETICS

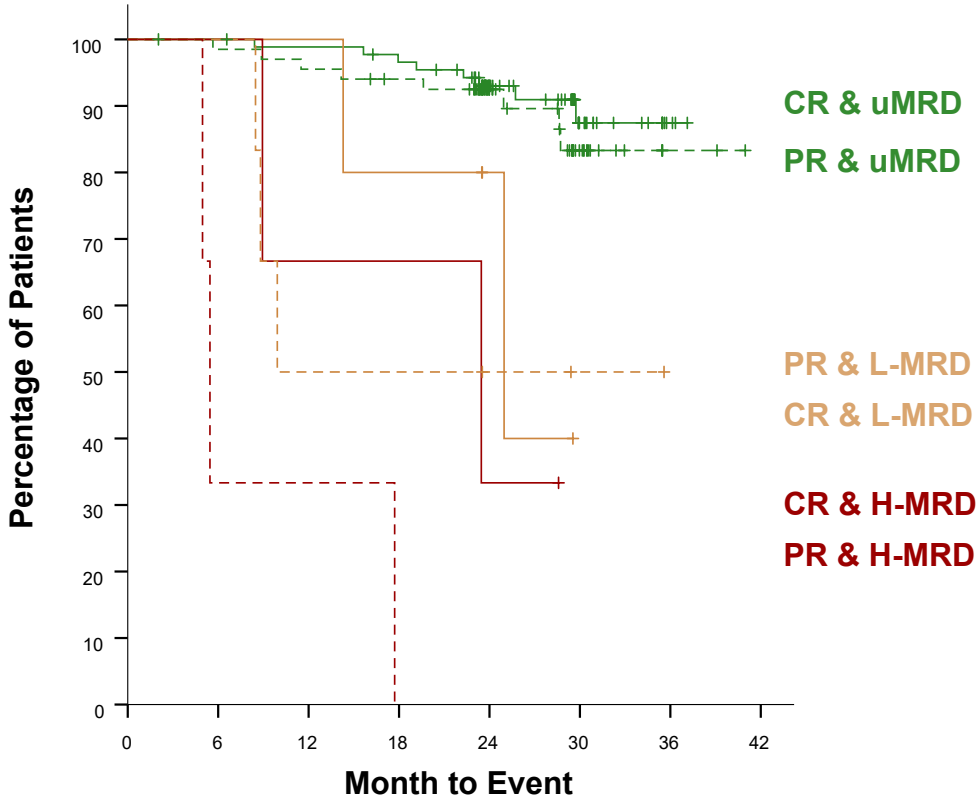
By PCR and NGS



# PFS LANDMARK ANALYSIS

According to response & MRD at end of Ven-Obi treatment

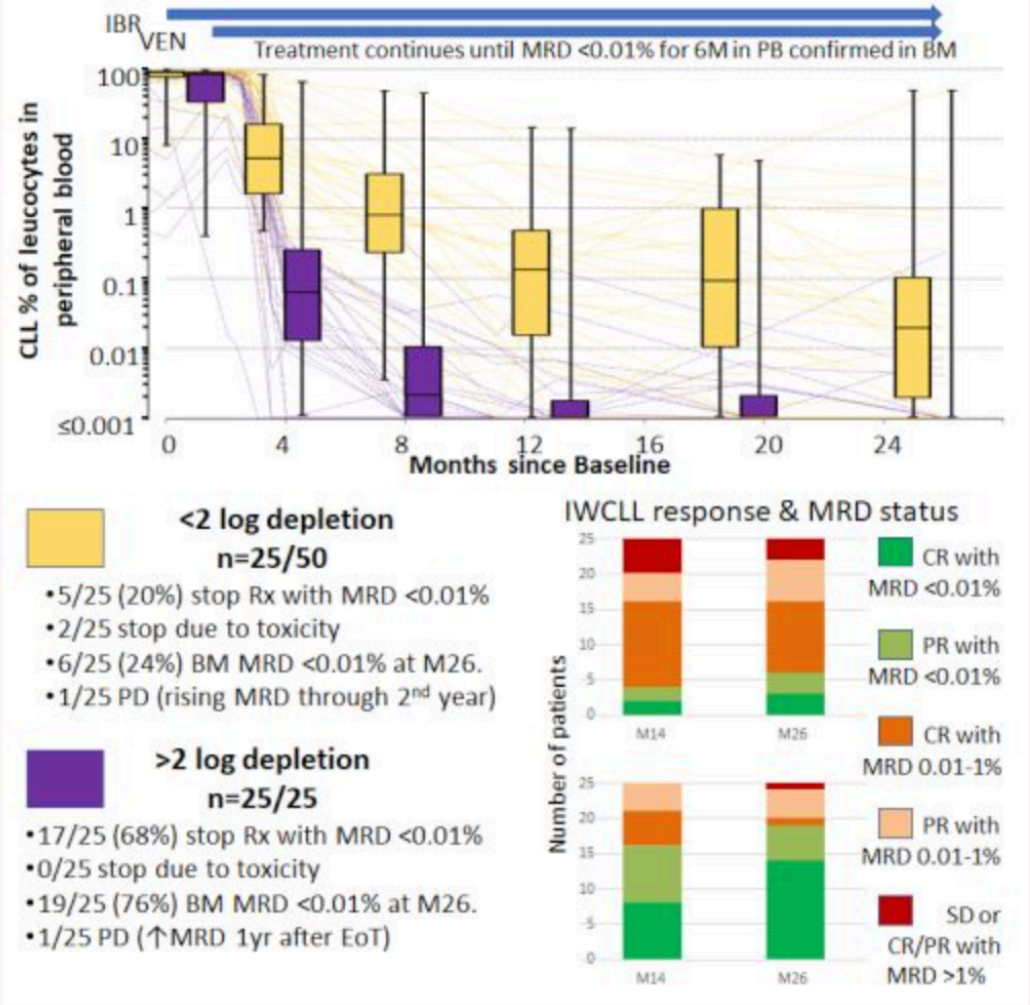


# KINETICS OF RESPONSE IN THE PERIPHERAL BLOOD PREDICTS LONG TERM RESPONSES TO IBRUTINIB + VENETOCLAX TREATMENT FOR RELAPSED/REFRACTORY CLL IN THE BLOODWISE TAP CLARITY TRIAL.

Author(s): Andy Rawstron, Nichola Webster, Surita Dalal, Kristian Brock, Francesca Yates, Chhaya Sankhalpara, Rebecca Boucher, Donald Macdonald, Christopher Fegan, Alison McCaig, Anna Schuh, Andrew Pettitt, John Gribben, Piers Patten, Stephen Devereux, Adrian Bloor, Christopher Fox, Francesco Forconi, Talha Munir, Peter Hillmen

**EHA Library. Rawstron A. 06/12/20; 294984; S164**

# CLARITY: Responses With 6 Mos of Ibrutinib → Ibrutinib + Venetoclax (until 2x time to MRD-neg.)



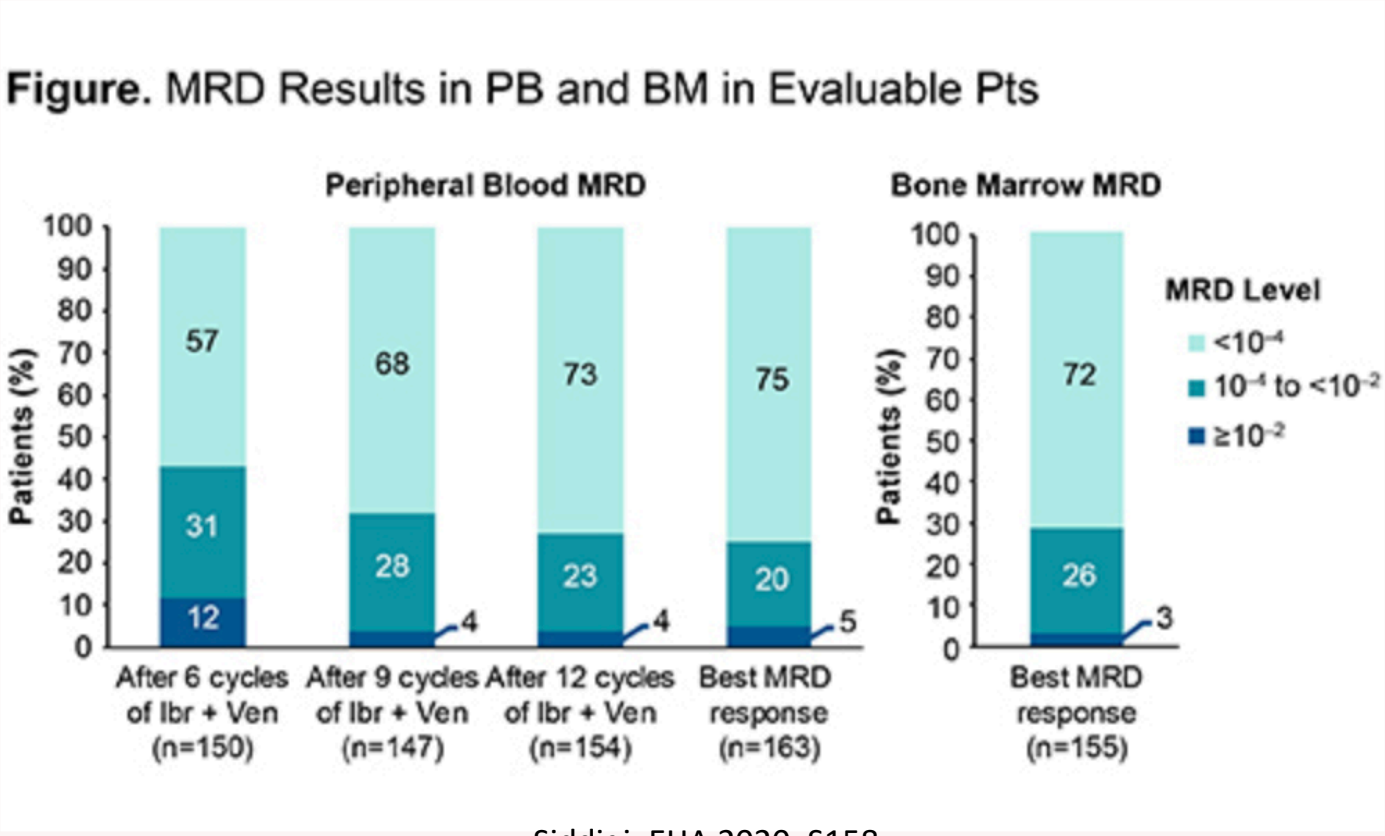

Rawstron et al., EHA 2020, S164

# FIRST-LINE IBRUTINIB (IBR) + VENETOCLAX (VEN) FOR PATIENTS (PTS) WITH CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)/SMALL LYMPHOCYTIC LYMPHOMA (SLL): EFFICACY AND SAFETY RESULTS FROM CAPTIVATE MRD COHORT

Author(s): Tanya Siddiqi, Constantine S. Tam, John N. Allan, Thomas J. Kipps, Stephen Opat, Alessandra Tedeschi, Paul M. Barr, Ryan Jacobs, Xavier C. Badoux, Bryone J. Kuss, Carol Moreno, Sharon Jackson, Livio Trentin, Paolo Ghia, Edith Szafer-Glusman, Cathy Zhou, Joi Ninomoto, James P. Dean, Danelle F. James, William G. Wierda

**EHA Library. Siddiqi T. 06/12/20; 294978; S158**

# CAPTIVATE trial: Ibrutinib lead in → Ibrutinib+Venetoclax



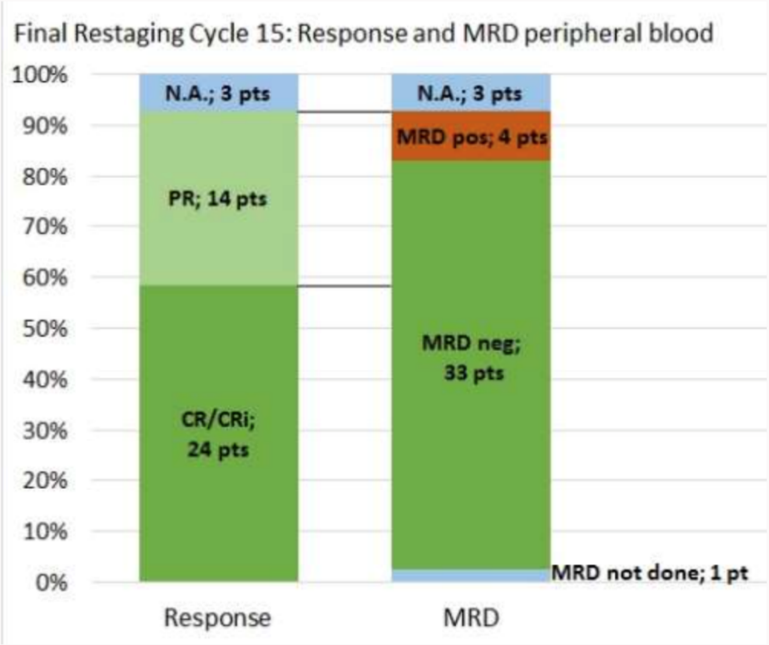

Siddiqi, EHA 2020, S158

# CLL2-GIVE, A PROSPECTIVE, OPEN-LABEL, MULTICENTER PHASE-II TRIAL OF OBINUTUZUMAB (GA101, G), IBRUTINIB (I), PLUS VENETOCLAX (VE) IN UNTREATED PATIENTS WITH CLL WITH 17P DELETION / TP53 MUTATION

Author(s): Henriette Huber, Simone Edenhofer, Julia von Tresckow, Michaela Grimm, Can Zhang, Sandra Robrecht, Moritz Fürstenau, Peter Dreger, Matthias Ritgen, Thomas Illmer, Lena Illert, Jan Dürig, Sebastian Böttcher, Carsten Niemann, Michael Kneba, Johannes Bloehdorn, Christof Schneider, Eugen Tausch, Anna-Maria Fink, Kirsten Fischer, Hartmut Döhner, Michael Hallek, Barbara Eichhorst, Stephan Stilgenbauer

EHA Library. Huber H. 06/12/20; 294977; S157

- Patients:
  - Between 09/2016 and 10/2018,
  - 41 pts (24 male, 17 female)
  - median age 62 (35 – 85) years,
  - Binet stage B/C 78.0%,
  - median CIRS score 3 (0-8),
  - Del(17p) in 26,
  - *TP53*mut in 39,
  - Unmutated IGHV in 32 pts.
- Results:
  - CR rate of 58.5% (24 pts)
  - PR rate 344.1% (14 pts)
  - Peripheral blood uMRD in 33 pts (80.5%).



# Summary

- EHA 2020: No practice-changing study.
- Confirmation of venetoclax combinations as very potent treatment concepts, yielding high MRD neg. remission rates in CLL.
- Ven-Obi slightly more potent that Ven-Ibru.

# CLL first line treatment (updated April 2020)

| Stage | del(17p) or p53mut | Fitness | IGVH | Therapy |
|---|---|---|---|---|
| Binet A-B, Rai 0-II, inactive disease | Irrelevant | Irrelevant | Irrelevant | None |
| Active disease or Binet C or Rai III-IV | Yes | Irrelevant | Irrelevant | Ibrutinib/Acalabrutinib or Venetoclax + Obinutuzumab or Idelalisib + Rituximab (if contraindications for ibrutinib)* |
| | No | Go go | M | FCR (BR above 65 years) or ibrutinib or Venetoclax + Obinutuzumab* |
| | | | U | Ibrutinib or FCR (BR above 65 years) or Venetoclax + Obinutuzumab* |
| | | Slow go | M | Venetoclax + Obinutuzumab or Chlorambucil + Obinutuzumab or Ibrutinib/Acalabrutinib* |
| | | | U | Venetoclax + Obinutuzumab or Ibrutinib/Acalabrutinib or Chlorambucil + Obinutuzumab* |

* Consider and discuss with patient: long-term vs fixed (6-12 m) duration therapy, lack of convincing evidence of overall survival differences, specific side effects of each therapeutic option (myelosuppression, infections, secondary malignancies for CIT; cardiac toxicity, bleeding and autoimmune disease for Ibru; TLS and infections for Ven-Obi; autoimmune disease (diarrhea) and opportunistic infections for Idelalisib).

# CLL 2L treatment February 2020

| Response to 1L Therapy | Fitness | Therapy |
|---|---|---|
| Refractory or progress within 3 years | Go go | Change to one of the following options: Ibrutinib, Idelalisib+R, Venetoclax+Rituximab, Chemoimmunotherapy (FCR or BR), Lenalidomide (+R), Alemtuzumab + Dexamethasone. Discuss consolidation with allogeneic SCT. |
| | Slow go | Change to one of the following options: Ibrutinib, Idelalisib + R, Venetoclax + Rituximab, Alemtuzumab + Dexamethasone, Chemoimmunotherapy (Chlorambucil + Rituximab or Obinutuzumab, BR, FCR-lite), Lenalidomide (+R), high-dose rituximab. |
| Progress after 3 years | All | Repetition of 1L therapy is possible. |