ASH 2020

CML ADVOCATES NETWORK CONFERENCE REPORT

Celia Marín, Head of Communications and Programme Manager
info@cmladvocates.net ***www.cmladvocates.nets***

62nd American Society of Hematology Congress

#ASH20

INTRODUCTION

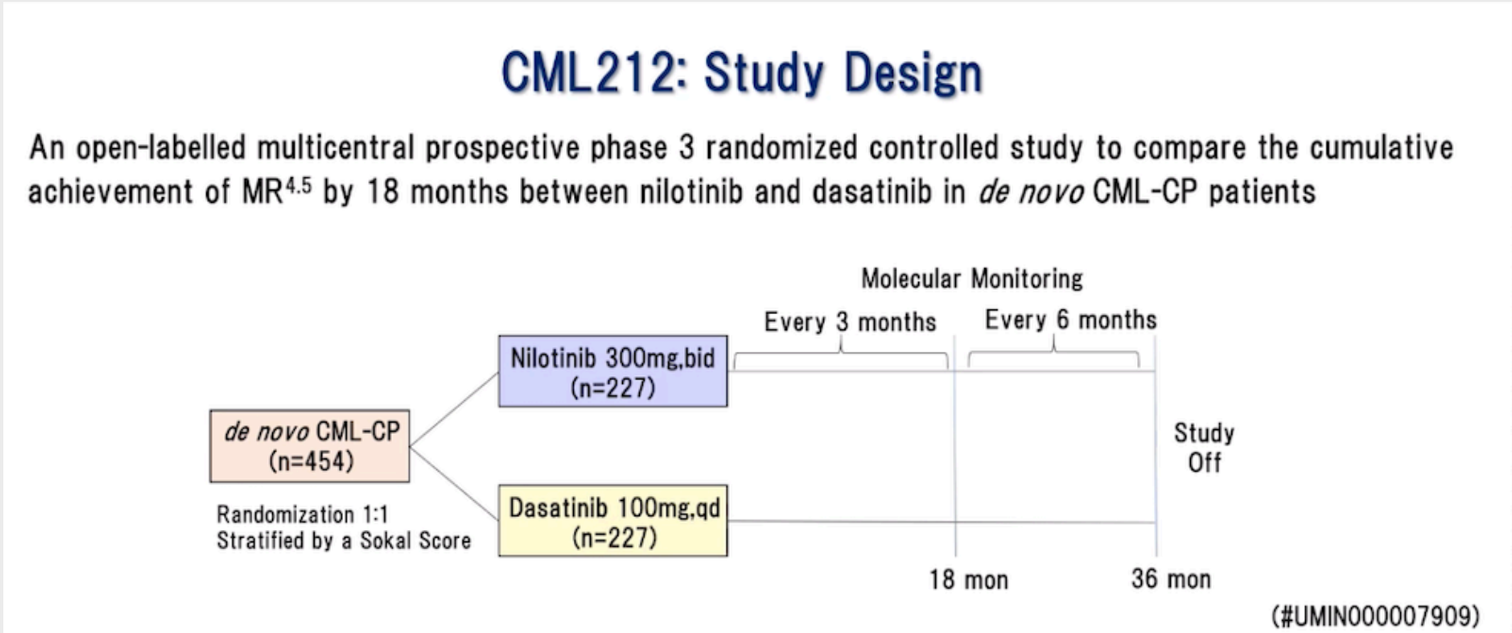
Originally to be held in San Diego, California, the 62nd ASH Annual Meeting and Exposition organised by the American Society of Hematology was presented as an all-virtual event on **December 5-8, 2020**, given the continuing threat of the COVID-19 pandemic.

This report summarizes the Chronic Myeloid Leukemia highlights presented in this key meeting for our community:

- 632 Chronic Myeloid Leukemia: Therapy– Building The Future CML.
- Education Program. Handling Challenging Questions in the Management of CML.
- 632: Chronic Myeloid Leukemia: Therapy: CML: New and Beyond.
- Special Interest Session: The 2020 Pandemic: Latest Insights on COVID-19.
- Education Program: Improving Symptom Control for Children with Hematological Malignancies.

632 Chronic Myeloid Leukemia: Therapy– Building The Future CML. Oral Abstracts

45 Nilotinib Vs. Dasatinib in Achieving MR4.5 for Newly Diagnosed Chronic Myeloid Leukemia: Results of the Prospective Randomized Phase 3 Study, JALSG CML212. Itaru Matsumura, MD, Ph.D.



Open-labelled multicentral prospective phase 3 randomised controlled study to compare the cumulative achievement of MR 4.5 by 18 months between nilotinib and dasatinib in *de novo* CML-CO patients.

Conclusions:

- Nilotinib and dasatinib were equally effective for de novo CML-CP patients in achieving MR 4.5 by 18 months (33% vs. 30,8% p=0,67) as well as achieving CCyR, MMR and MR 4.0 in terms of both frequencies and times to achievement.
- The continuity of nilotinib and that of dasatinib were almost the same at 36 months.
- No unknown serious adverse event was observed during the study.

632 Chronic Myeloid Leukemia: Therapy– Building The Future CML. Oral Abstracts

46 Bosutinib (BOS) Versus Imatinib for Newly Diagnosed Chronic Phase (CP) Chronic Myeloid Leukemia (CML): Final 5-Year Results from the Before Trial. Tim H Brümmendorf, MD.

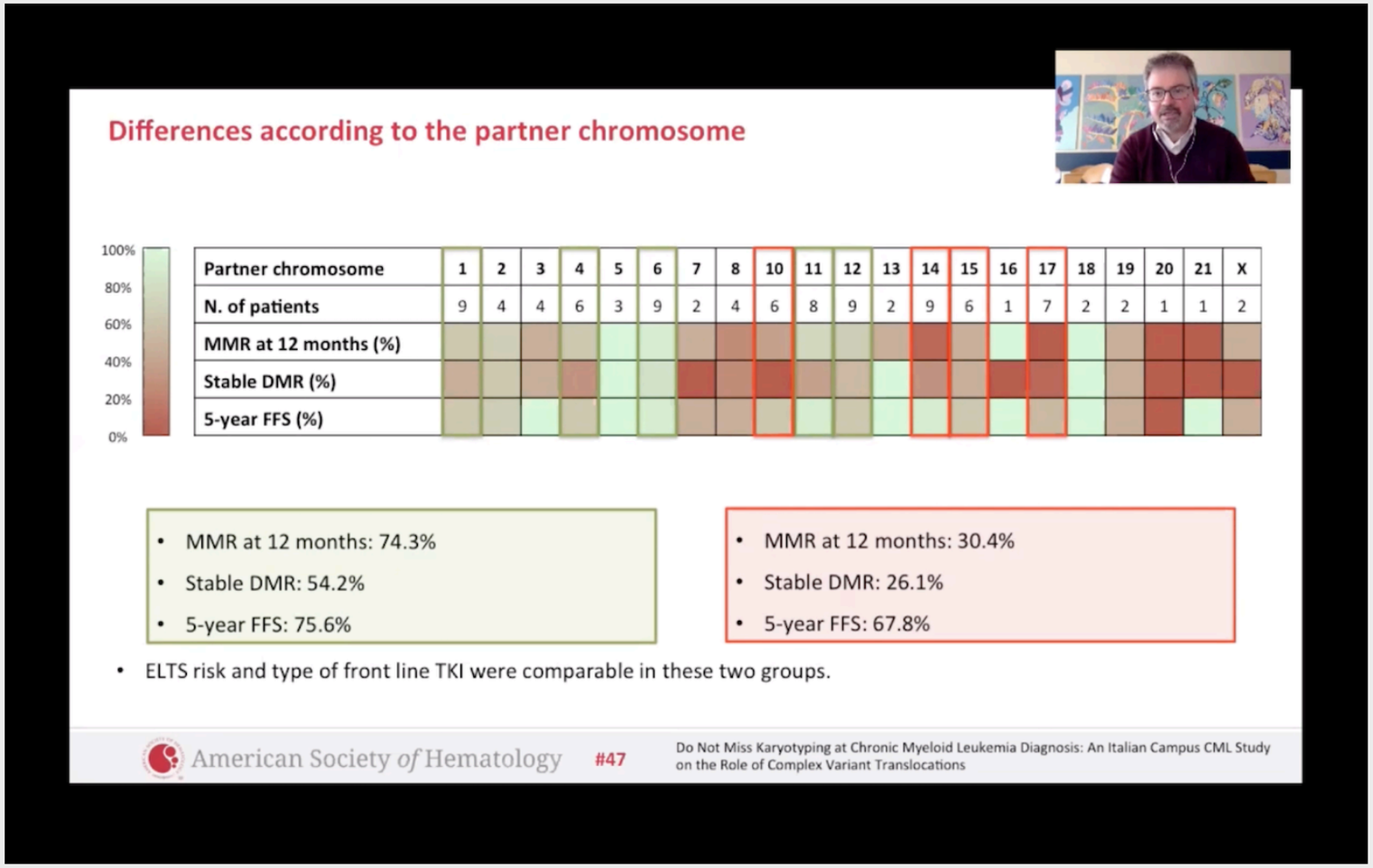
Open-label, randomized, multicenter, phase 3 trial to evaluate the efficacy in the ITT population with the exception of cytogenetic endpoints which were evaluated in the modified ITT population .

Conclusions:

- After 5 years of follow-up, bosutinib continued to demonstrate superior efficacy compared with imatinib.
- The greatest improvement in MR with bosutinib was observed in Sokal high-risk patients.
- A higher percentage of patients achieved BCR-ABL1 transcripts ≤10% at 3 months in the bosutinib vs the imatinib arm.
- A substantial proportion of patients receiving bosutinib or imatinib achieved a 2-year sustained MR4.
- Long-term AEs were generally manageable.
- These results confirm the use of bosutinib as a standard of care in patients with newly diagnosed CP CML.

632 Chronic Myeloid Leukemia: Therapy– Building The Future CML. Oral Abstracts

47 Do Not Miss Karyotyping at Chronic Myeloid Leukemia Diagnosis: An Italian Campus CML Study on the Role of Complex Variant Translocations. Massimiliano Bonifacio, MD.



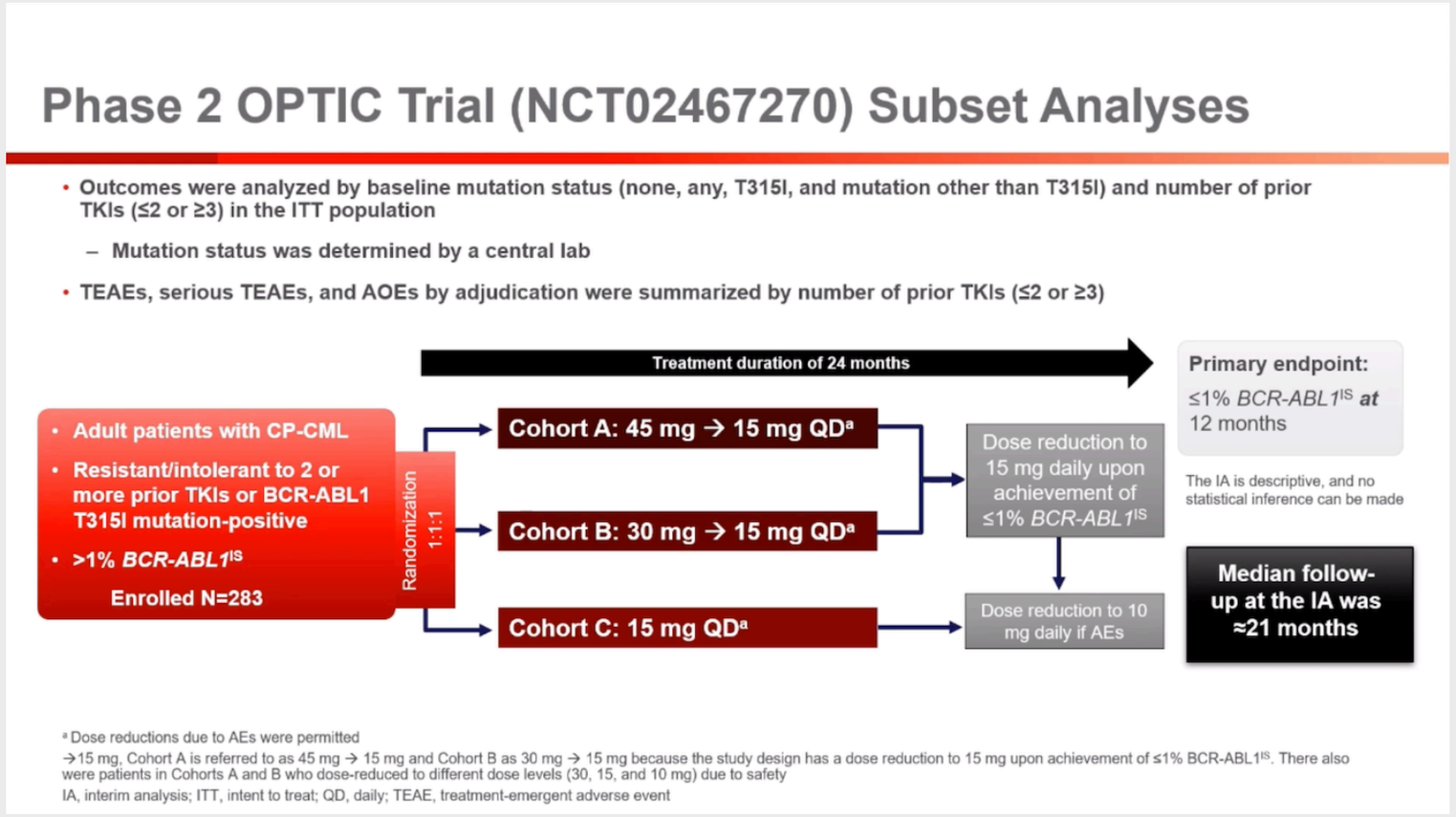
Study to describe the characteristics of patients with CVT in a large cohort of CML patients in 19 Italian Centers and to explore the impact of the different partner chromosomes on outcome.

Conclusions:

- CML patients with complex variant translocations treated with 2G-TKI front line had higher rates of optimal responses at 3 and 6 months as compared to patients treated with imatinib.
- However, molecular responses at 12 months and beyond did not differ according to front line TKI.
- Differences in response and long-term outcome depending on partner chromosome were observed, regardless of risk and front line TKI.
- Data reinforce the usefulness of bone marrow karyotyping in CML.

632 Chronic Myeloid Leukemia: Therapy– Building The Future CML. Oral Abstracts

48 Outcome By Mutation Status and Line of Treatment in Optic, a Dose-Ranging Study of 3 Starting Doses of Ponatinib in Patients with CP-CML. Jorge E. Cortes, MD.

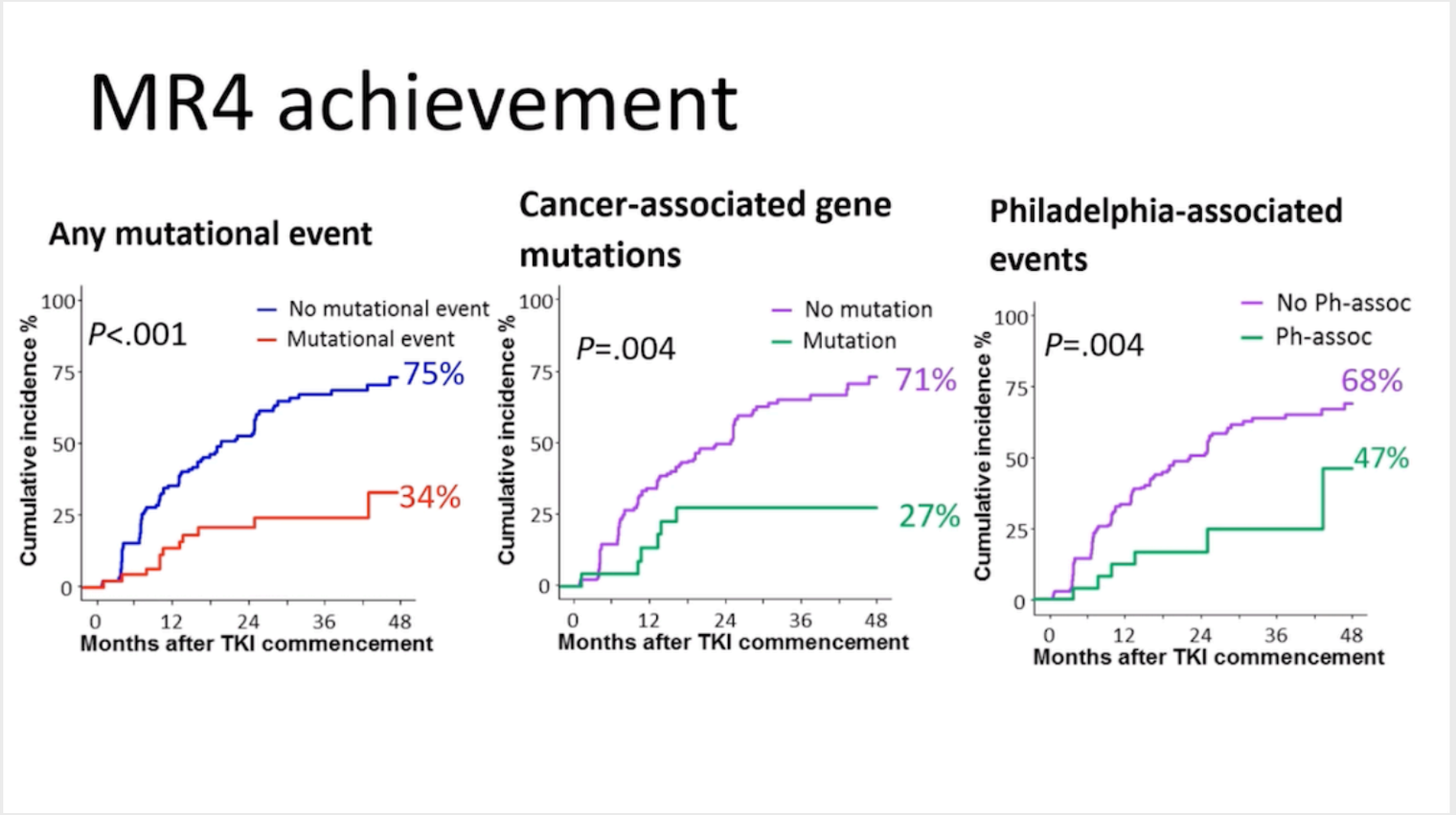


Conclusions:

- OPTIC IA shows the benefit of ponatinib in all 3 dosing regimens in a largely resistant population where the majority of patients (>60%) failed to achieve a response greater than CHR on immediate prior therapy
- In resistant patients with or without mutations, the rate of ≤1% BCR-ABL1 by 12 months was highest in Cohort A (45mg starting dose) with the most notable differences seen in patients with T315I mutation.
- Use of ponatinib in earlier lines of therapy provides an optimal benefit:risk profile with a potential trend toward better outcomes for patients previously treated with ≤ TKIs.

632 Chronic Myeloid Leukemia: Therapy– Building The Future CML. Oral Abstracts

49 Mutated Cancer-Related Genes Detected at Diagnosis of CML and a Novel Class of Variant Associated with the Philadelphia Translocation Are Both Independent Predictors of Inferior Outcomes. Naranie Shanmuganathan, FRACP, FRCPA, MBBS.

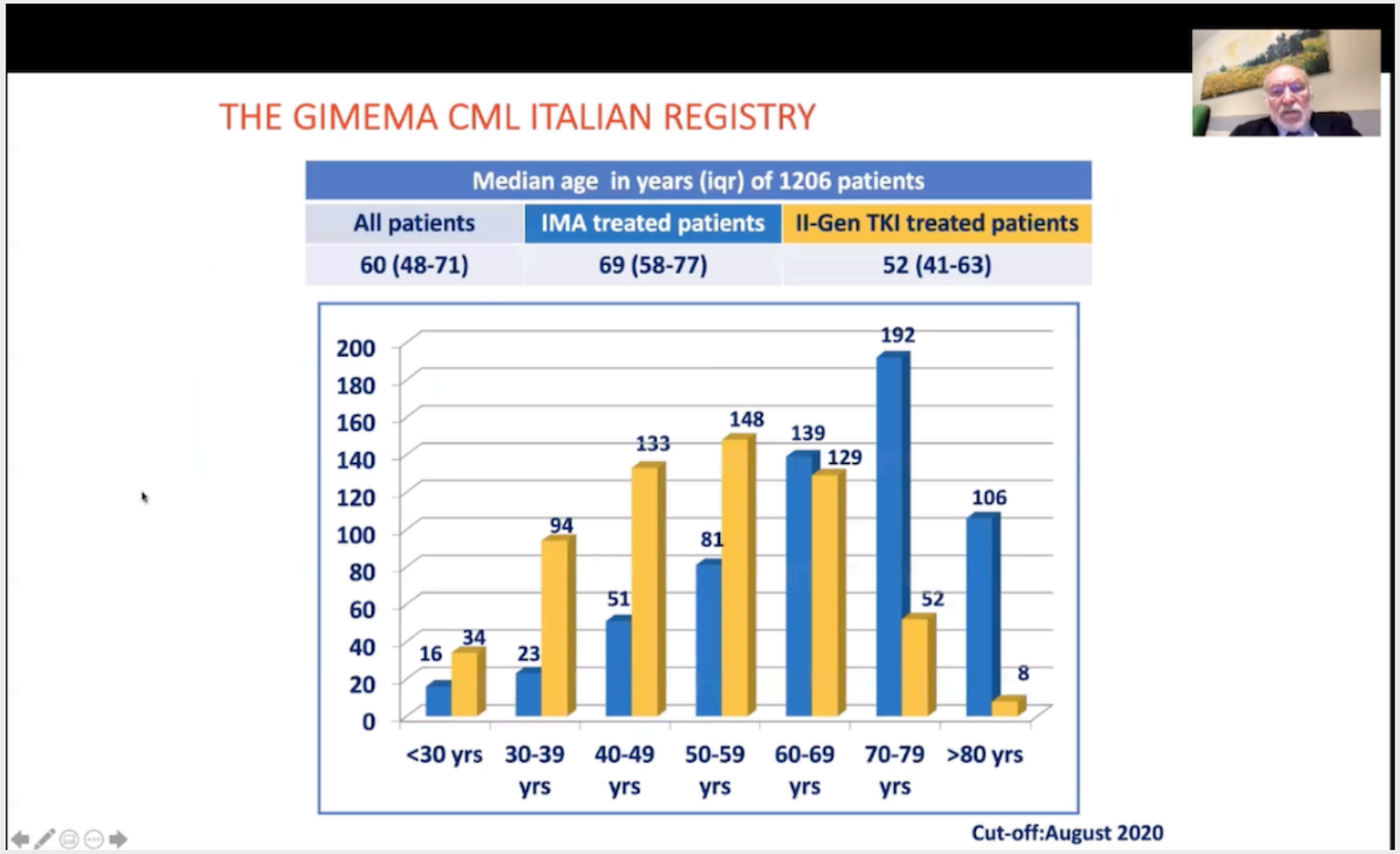


Conclusions:

- 28% of patients will have a mutational event:
    - 16% cancer related gene mutation
    - 16% Ph-associated events.
- Cancer associated gene mutations and Ph-associated events are predictive for progression to accelerated and blast crisis, but also kinase domain mutation development in addition to inferior molecular responses.
- Ph-associated events are specifically associated with inferior EMR achievement and slower BCR-ABL1 decline.

632 Chronic Myeloid Leukemia: Therapy– Building The Future CML. Oral Abstracts

50 Predictive Factors for Overall Survival in Chronic Myeloid Leukemia Patients: An Analysis By the Gimema Cml Italian Study. Patrizia Pregno.



Conclusions:

- Results show a different clinical behaviour among Italian physicians who prevalently prescribed IMA to older patients with comorbidities as compared to 2gen TKIs, more frequently used in younger and healthier patients.

- Percentage of CML related deaths decreases with age and in presence of comorbidity.

- A comparison between treatments in the whole cohort suggests a better OS for 2gen TKI vs IMA. However, in patients without comorbidity any difference in OS is confirmed.

- Prognostic baseline features associated to OS were age, comorbidity and the ELTS score, that shows a much stronger prediction on OS in patients without comorbidities.

Education Program. Handling Challenging Questions

First Generation vs. Second Generation TKI - Which is Best At Diagnosis of Chronic Phase CML? Vivian G. Oehler, MD.

This first session of the education program was focused on: identifying disease-specific risk factors at chronic phase diagnosis that influence first-line tyrosine kinase inhibitor selection; examine how first-line TKI selection impacts outcomes; and delineate patient comorbidities that impact first-line TKI selection.

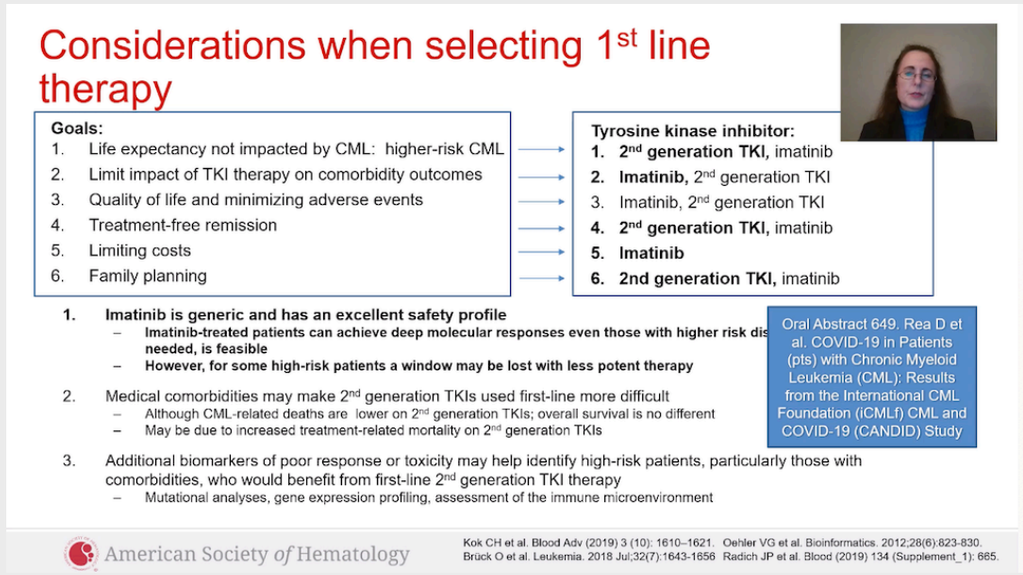
When is it safe to stop TKIs? Delphine Rea, MD, Ph.D.

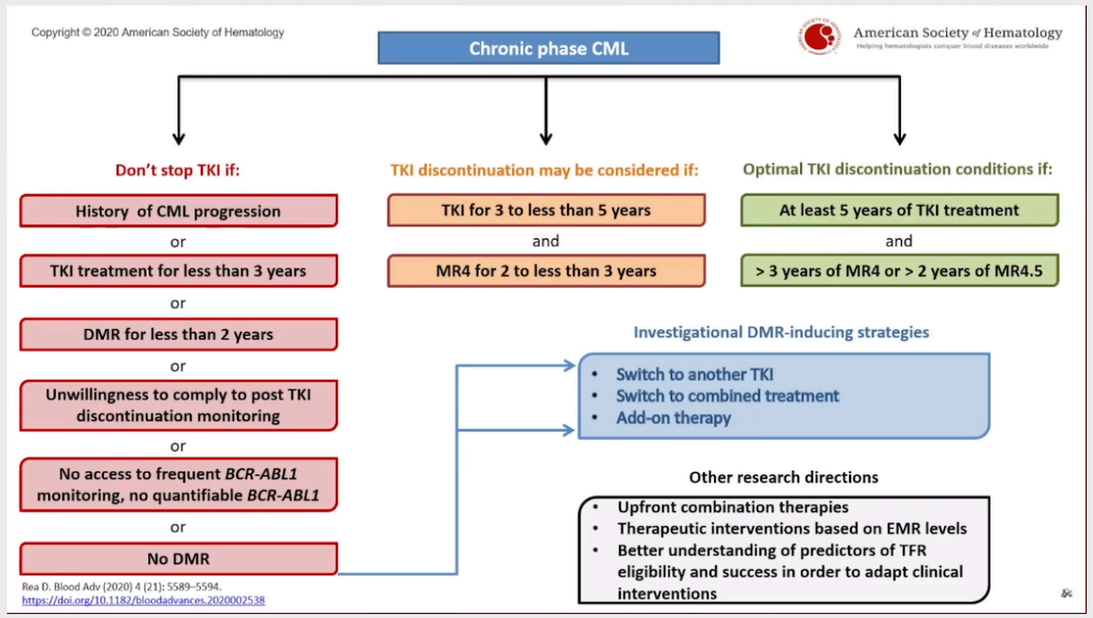
The second session run by Dr. Rea was through the knowledge on:

Factors influencing deep molecular responses achievement

The appropriate patient selection for TKI discontinuation

And finally, the safety aspects after treatment ends.



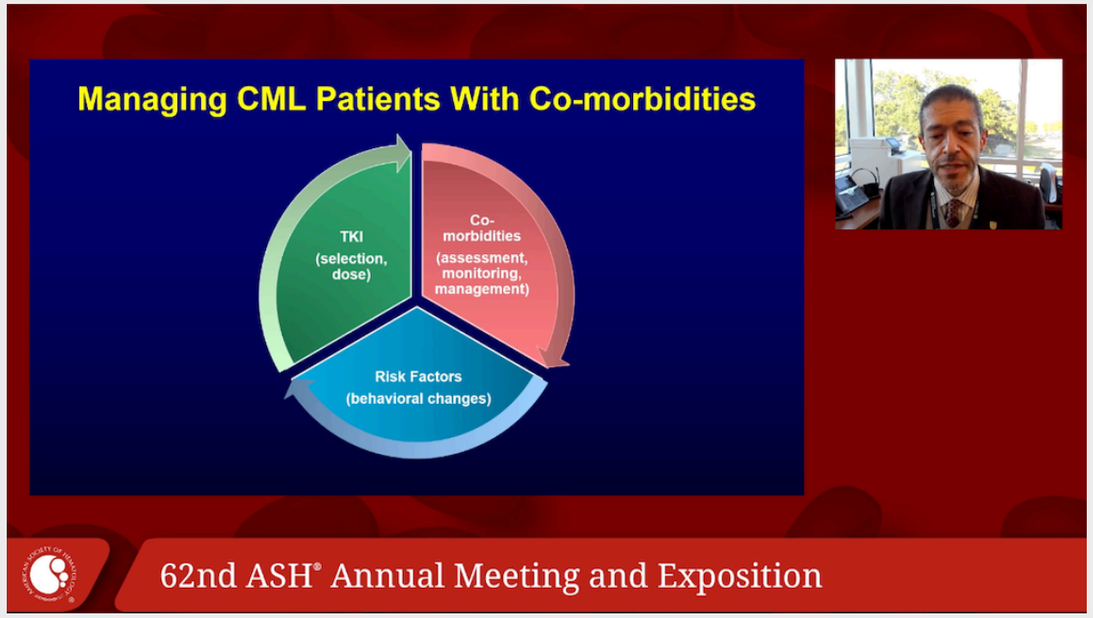


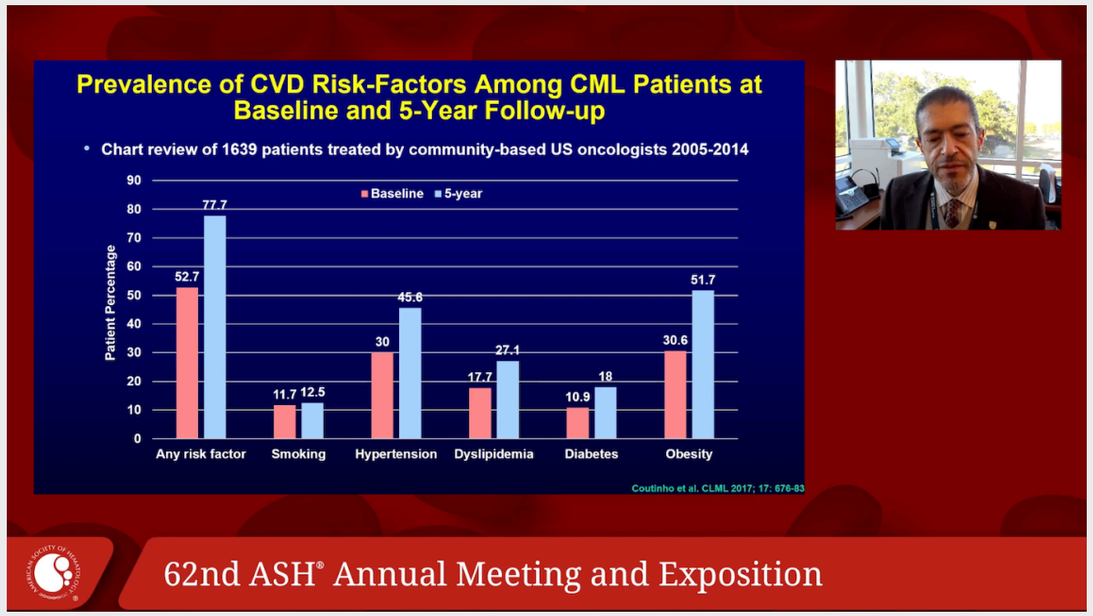
Education Program. Handling Challenging Questions

How to manage CML patients with comorbidities? Jorge E. Cortes, MD.

The last session of the education program with Dr. Cortés as speaker gave us key advises on managing CML patients with comorbidities as the following:

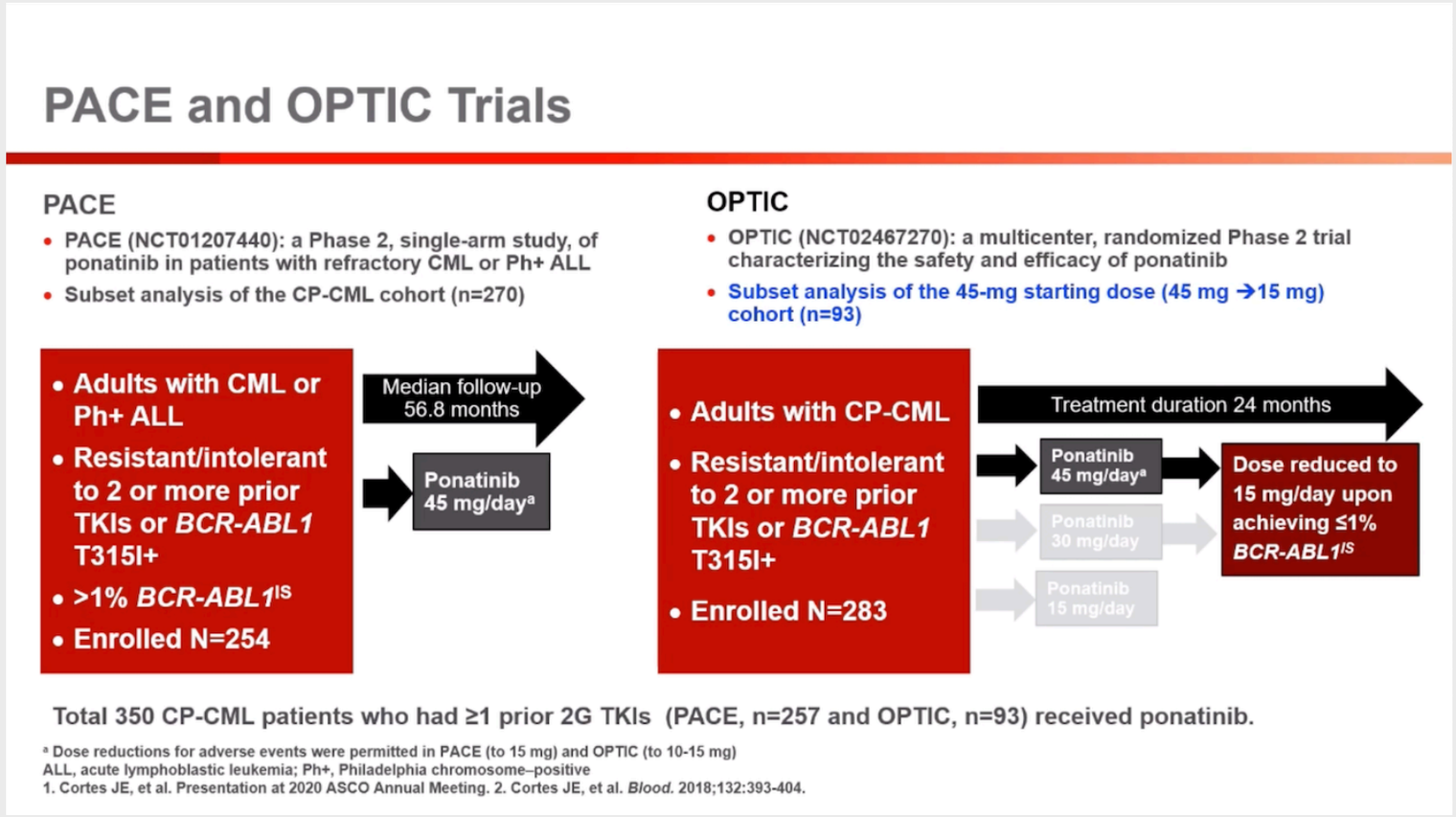
- Assess risk factors
- Eliminate/manage behavioural risk factors (smoking, diet, exercise)
- Aggressively follow and manage co-morbidities (DM, hypertension, cholesterol, weight)
- When possible, use drugs with lower risk for patients at higher risk
- Dose adjustments as needed
- Monitor ankle-brachial index, statins?
- Involve specialists early and balance risk:benefit





632: Chronic Myeloid Leukemia: Therapy: CML: New and Beyond, Oral Abstracts.

647 Efficacy and Safety of Ponatinib (PON) in Patients with Chronic-Phase Chronic Myeloid Leukemia (CP-CML) Who Failed One or More Second-Generation (2G) Tyrosine Kinase Inhibitors (TKIs): Analyses Based on PACE and Optic. Hagop M. Kantarjian, MD.

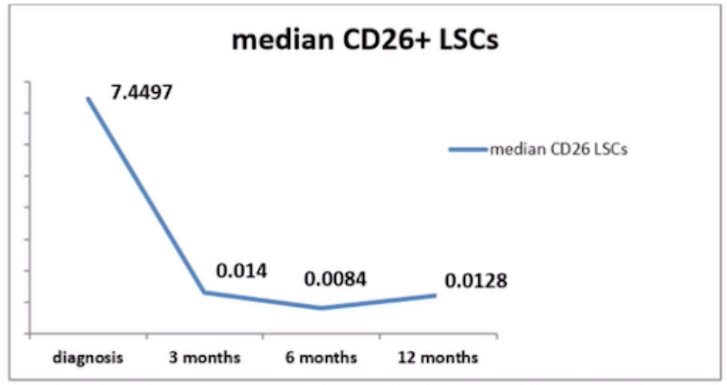


Conclusions:

- In this analysis, ponatinib shows high response rates and robust survival outcomes in patients who have failed prior 2G TKI.
- Compared with PACE, the overall incidences of AOEs and serious TEAEs as well as exposure-adjusted AOEs during the first 2 years were lower in OPTIC.
- Ponatinib demonstrated a favorable benefit:risk profile among all TKIs for resistant CP-CML patients who have failed prior 2G TKI(s) regardless of mutation status.

632: Chronic Myeloid Leukemia: Therapy: CML: New and Beyond, Oral Abstracts.

648 Peripheral Blood CD26+ Leukemia Stem Cells Monitoring in Chronic Myeloid Leukemia Patients from Diagnosis to Response to TKIs: Interim Results of a Multicenter Prospective Study (PROSPECTIVE FLOWERS). Monica Bocchia.



Circulating CD26+ LSCs decrease rapidly after 3 months of TKI treatment, afterward fluctuating at very low level in the great majority of patients

	CD26 LSCs at diagnosis median values	CD26 LSCs at +3 months median values	CD26 LSCs at +6 months median values	CD26 LSCs at +12 months median values
IMATINIB	4.5818 (0.1452-487)	0.01175 (0-6.4901)	0.009 (0-0.142)	0.0114 (0-0.1017)
NILOTINIB	12.4801 (0.0126-3643)	0.01655 (0-1.787)	0.0059 (0-0.132)	0.0107 (0-0.1824)
DASATINIB	17.3378 (0,2993-365)	0.0089 (0-0.2164)	0.0052 (0-1.1889)	0.009 (0-0.0765)

No substantial differences between TKIs

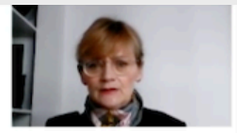
American Society of Hematology

Conclusions:

- They confirmed no correlation between the absolute number of persisting CD26+ LSCs and BCR-ABL copies.
- However, patients with failure or suboptimal response leading to a switch of TKI showed the highest amount of circulating CD26+LSCs at diagnosis.
- They found a potential correlation between younger age and higher number of circulating CD26+LSCs at diagnosis that needs further elucidation.

632: Chronic Myeloid Leukemia: Therapy: CML: New and Beyond, Oral Abstracts.

649 COVID-19 in Patients (pts) with Chronic Myeloid Leukemia (CML): Results from the International CML Foundation (iCMLf) CML and COVID-19 (CANDID) Study. Delphine Rea, MD, PhD.



Patient characteristics

Characteristics (n=201)	Results n, (%)
Male sex	122 (60.7%)
Median age	53 years (range 18-89)
Median duration of CML (range)	70 months (0-336)* *10 newly diagnosed CML pts
CML treatment at the time of COVID-19	
- Hydroxyurea	2 (1%)
- IFN	1 (0.5%)
- TKI	162 (81.5%)
- None**	34 (17%)
TKI type among TKI-treated pts (n=162)	
Imatinib	91 (56.2%)
2nd generation TKI	64 (39.5%) (dasatinib 29 / bosutinib 11 / nilotinib 24)
Ponatinib	5 (3,1%)
Experimental TKI (HQP1351)	1 (0.6%)
Unknown	1 (0.6%)

** 14 pts in TKI-free remission
8 pts newly diagnosed
5 pts with safety issues
2 TFR post allo SCT
3 other causes

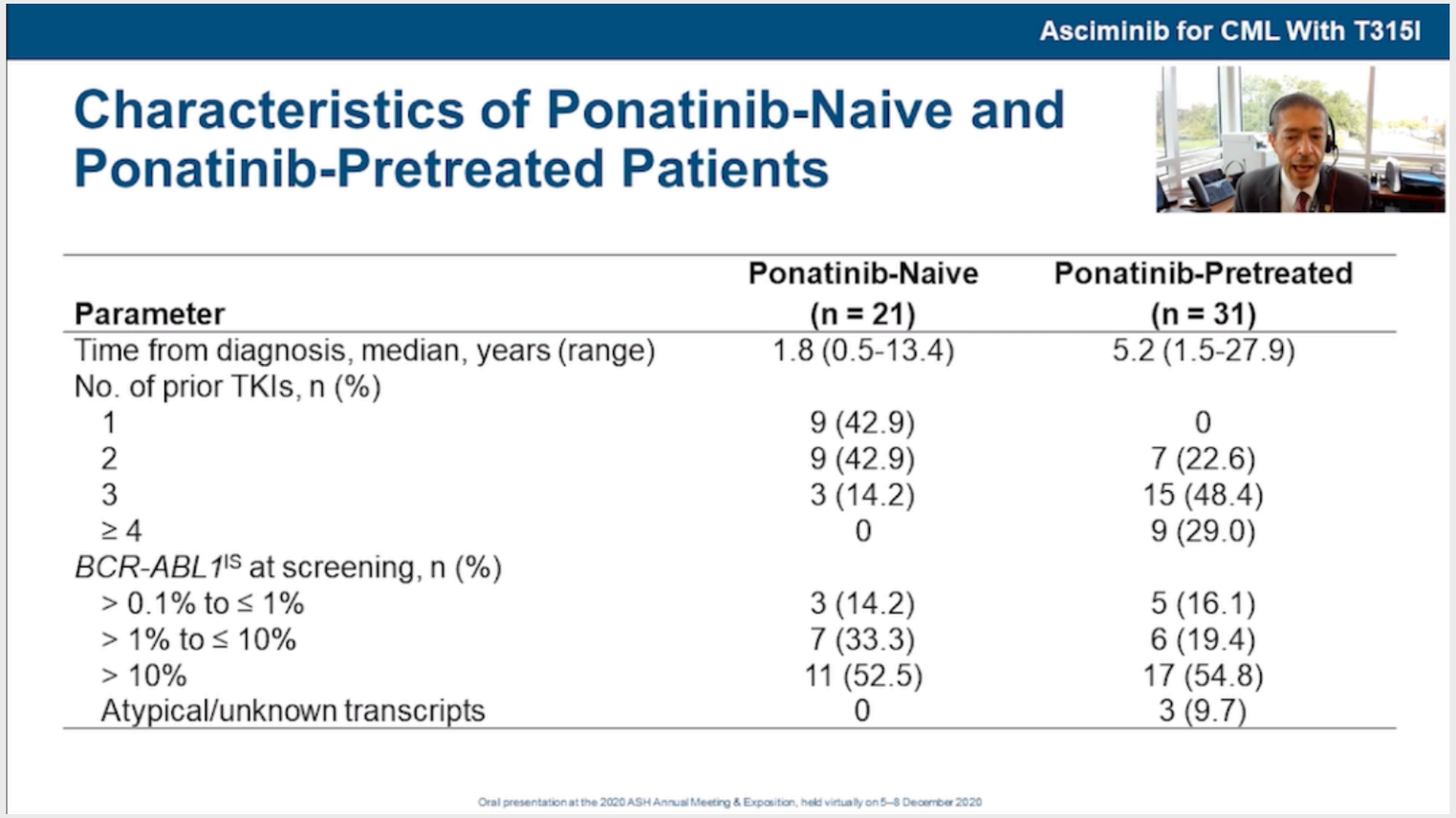
American Society of Hematology

Conclusions:

- SARS CoV-2 infection may be asymptomatic in CML patients.
- Symptomatic COVID-19 in CML is mild to moderate in the majority (~80%) of patients.
- Half of CML patients with severe/ critical COVID-19 died.
- The main factor associated with COVID-19 severity is older age, rather than CML.
- TKI treatment and generation do not seem to be associated with COVID-19 severity or death.
- Altogether, these data suggest that CML may not represent a particular vulnerability although few exceptions may exist.

632: Chronic Myeloid Leukemia: Therapy: CML: New and Beyond, Oral Abstracts.

650 Asciminib, a First-in-Class STAMP Inhibitor, Provides Durable Molecular Response in Patients (pts) with Chronic Myeloid Leukemia (CML) Harboring the T315I Mutation: Primary Efficacy and Safety Results from a Phase 1 Trial. Jorge E. Cortes, MD.



Conclusions:

- Asciminib 200 mg BID has a favorable safety profile and meaningful clinical efficacy in patients with the T315I mutation.
- Nearly half of patients achieved MMR, which has been durable in most of the patients.
- The safety profile of asciminib 200 mg BID is consistent with that observed at a lower dose in patients without the T314I mutation.
- Asciminib is a promising therapeutic option for patients with CML-CP/AP with the T351I mutation, including those for whom ponatinib treatment has failed.

632: Chronic Myeloid Leukemia: Therapy: CML: New and Beyond, Oral Abstracts.

651 Novel BCR-ABL1 Tyrosine Kinase Inhibitor (TKI) HQP1351 (Olverembatinib) Is Efficacious and Well Tolerated in Patients with T315I-Mutated Chronic Myeloid Leukemia (CML): Results of Pivotal (Phase II) Trials. Qian Jiang, MD.

Conclusions:

- HQP1351 was highly efficacious and well tolerated in the TKI-resistant CML-CP and CML-AP patients with T351I mutation(s) in the pivotal Phase II studies.

652 Phase 1 Trial of Vodobatinib, a Novel Oral BCR-ABL1 Tyrosine Kinase Inhibitor (TKI): Activity in CML Chronic Phase Patients Failing TKI Therapies Including Ponatinib. Jorge E. Cortes, MD.

Conclusions:

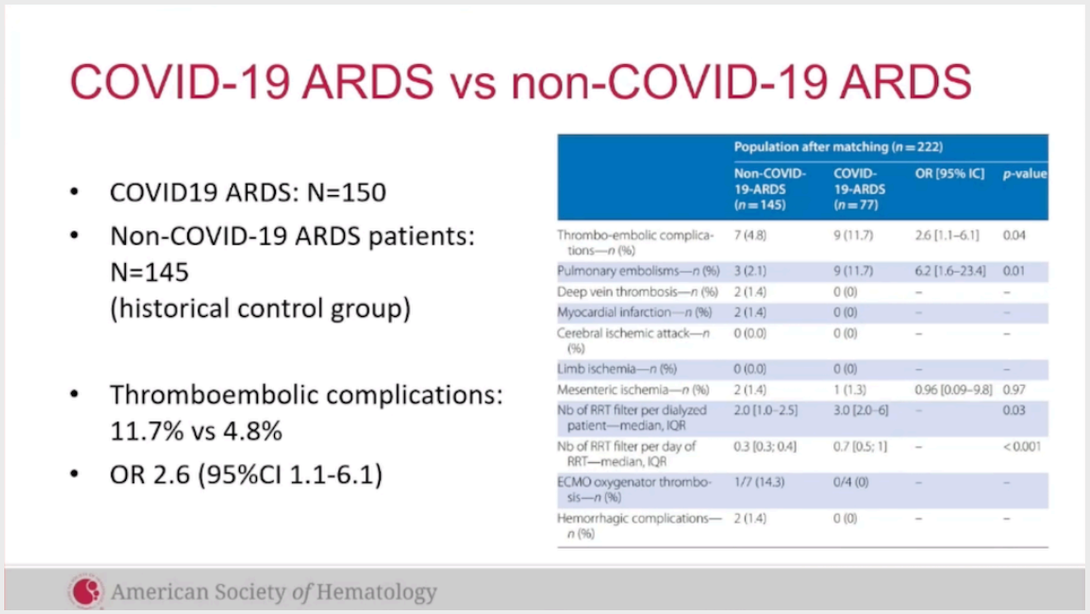
- Efficacy was comparable in both ponatinib naïve and ponatinib treated groups with durable responses.
- Notable efficacy in ponatinib treated patients despite being more heavily pre-treated.
- Well tolerated safety profile in both treatment groups.

Special Interest Session: The 2020 Pandemic: Latest Insights on COVID-19.

Do COVID-19 Patients Face Increased Risk of Thrombosis? Saskia Middeldorp, MD, PhD.

Dr. Middledorp explained the risk of venous thromboembolism in #COVID19 patients, making a comparison between them and other critically ill patients.

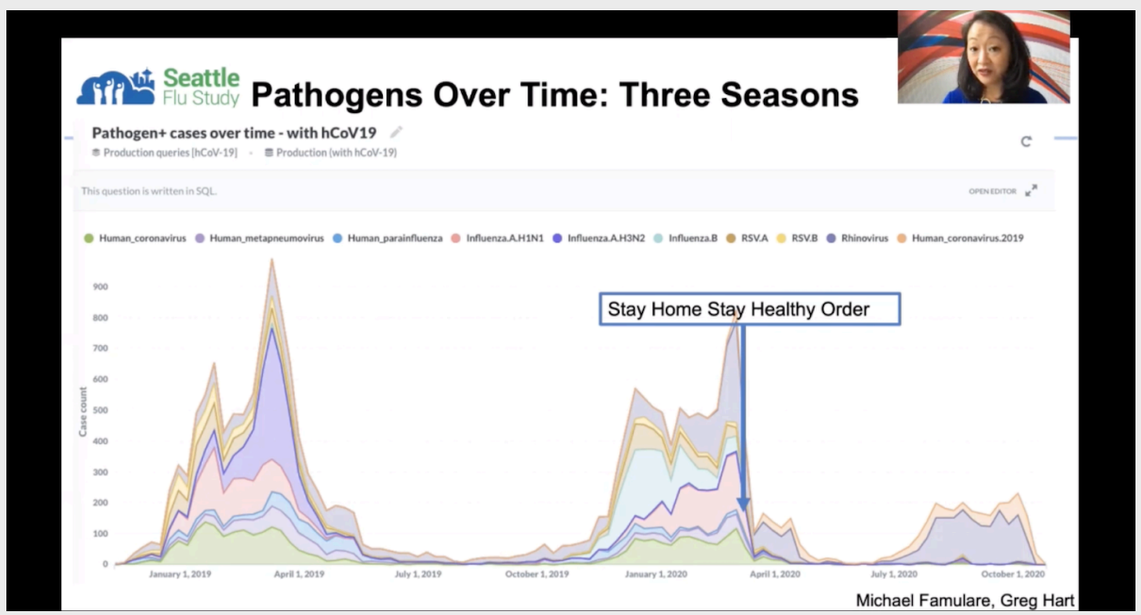
Conclusion: Patients with COVID19 coagulopathy are at a higher risk of thrombosis and death.



How Can Community-Based Surveillance Strategies for Sars-Cov-2 Inform Pandemic Planning? Helen Chu, MD, MPH.

Conclusions of this interesting session were:

- Biospecimen repositories linked with clinical data are essential for real-time identification of novel pathogens.
- Community-based studies provide an opportunity to identify pathogens early and take steps to prevent further transmission.



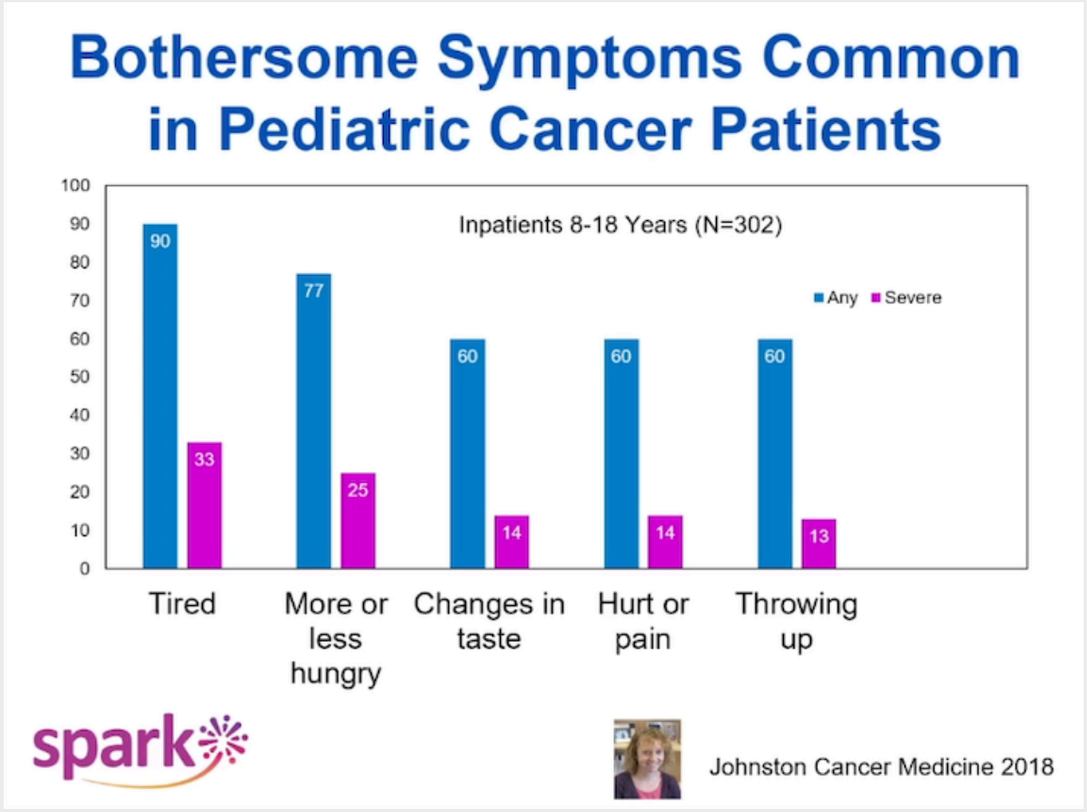
Education Program: Improving Symptom Control for Children with Hematological Malignancies.

Symptom Screening in Routine Care - Time to Move Beyond Research? Lillian Sung, MD,PhD

Dr. Sung described the importance of symptom control in children with cancer, and approaches to identify symptoms amenable to clinical implementation.

Conclusions

- Symptoms prevalent and severely bothersome in pediatric cancer
- SPARK: Routine symptom screening, symptom feedback and care pathways.
- Multicenter trials to identify optimal strategies



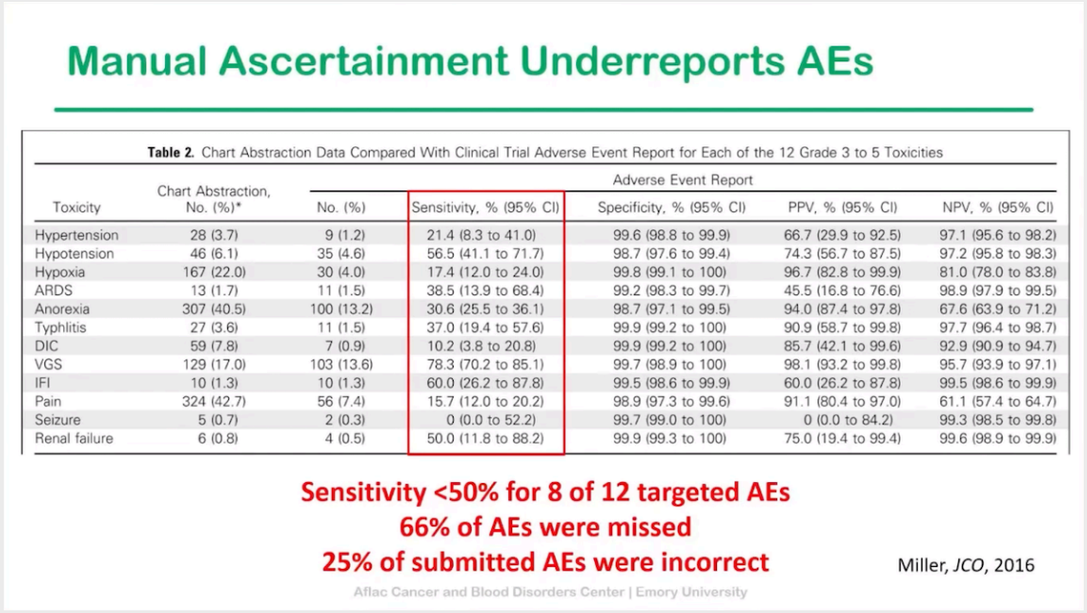
Education Program: Improving Symptom Control for Children with Hematological Malignancies.

Capturing Treatment Toxicities in Clinical Practice. Tamara P. Miller, MD,MSc

Dr. P. Miller explained the current methods of capturing treatment toxicities on pediatric hematology clinical trials , concerns about accuracy of adverse event (AE) reporting and the specific challenges related to pediatric trials.

Conclusions:

- AE reporting is currently performed manually
- AEs are underreported and have inaccuracies
- Wide-ranging challenges exist that prevent accurate capture
- Automated ascertainment of AEs will be crucial to improving upon the current system of AE reporting and toxicity capture for patients on study and in clinical practice.

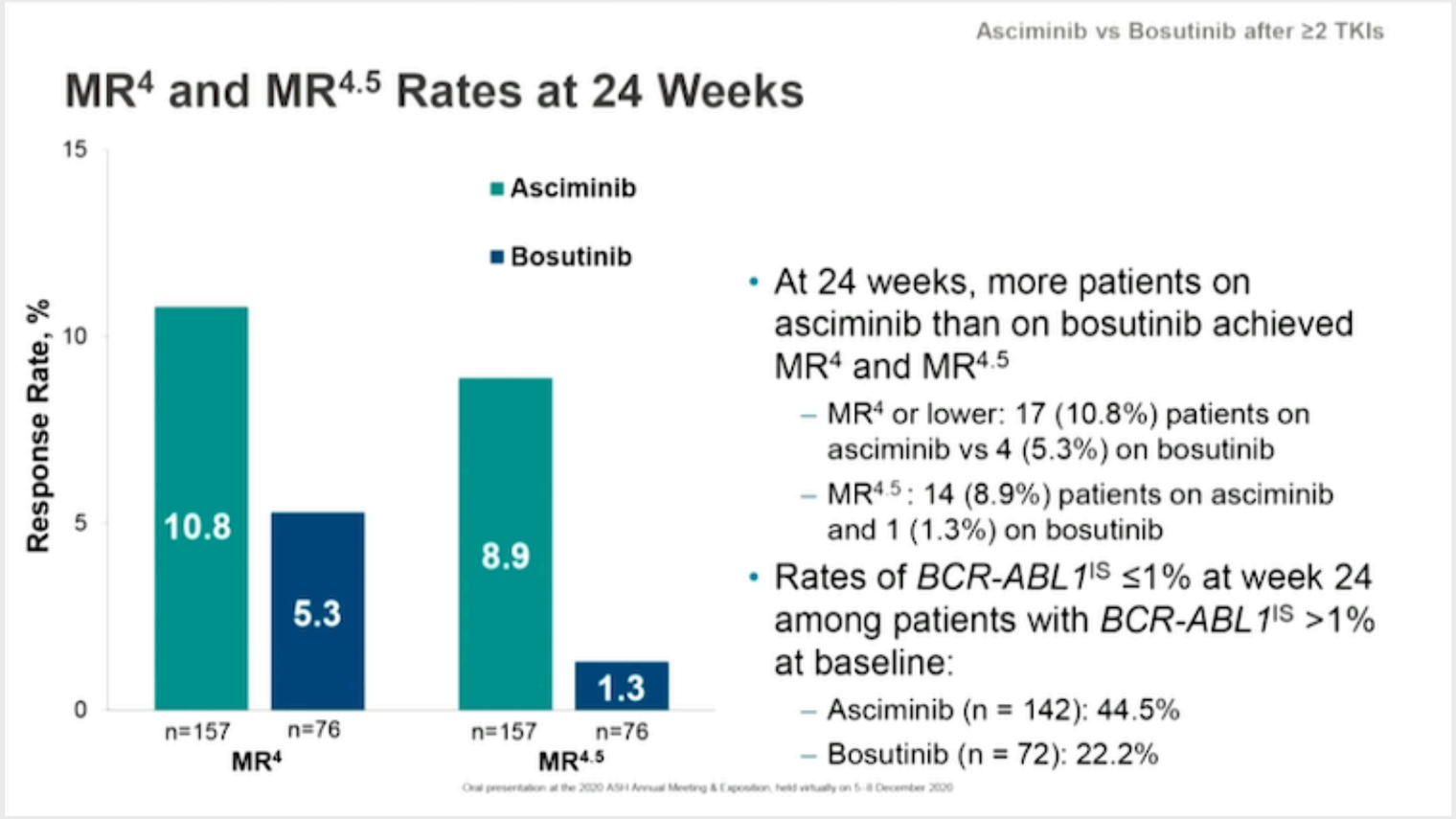


Interventions to Improve Symptoms. Robert Phillips, MD.

In this session about improving symptom control with children with haematological malignancies, different approaches to control toxicity and aversive symptoms were discussed, from preventative strategies to therapeutic approaches.

Late-Breaking Abstracts Session

LBA-4 Efficacy and Safety Results from ASCEMBL, a Multicenter, Open-Label, Phase 3 Study of Asciminib, a First-in-Class STAMP Inhibitor, vs Bosutinib (BOS) in Patients (Pts) with Chronic Myeloid Leukemia in Chronic Phase (CML-CP) Previously Treated with ≥2 Tyrosine Kinase Inhibitors (TKIs. *Andreas Hochhaus, MD*.



Conclusions:

- Asciminib demonstrated statistically significant and clinically meaningful, superior efficacy compared with bosutinib and a favorable safety profile.
- The ASCEMBL results support the use of asciminib as a new treatment option in CML, particularly in patients with resistant/intolerance to ≥2 TKIs.
- BCR-ABL1 remains the key driver of CML even in 3L+ patients; asciminib has demonstrated a favorable benefit:risk profile in this patient population by its unique ability to Specifically Target the ABL1 Myristoyl Pocket (STAMP).

ASH 2020

CML ADVOCATES NETWORK CONFERENCE REPORT

Celia Marín, Head of Communications and Programme Manager
info@cmladvocates.net ***www.cmladvocates.net***