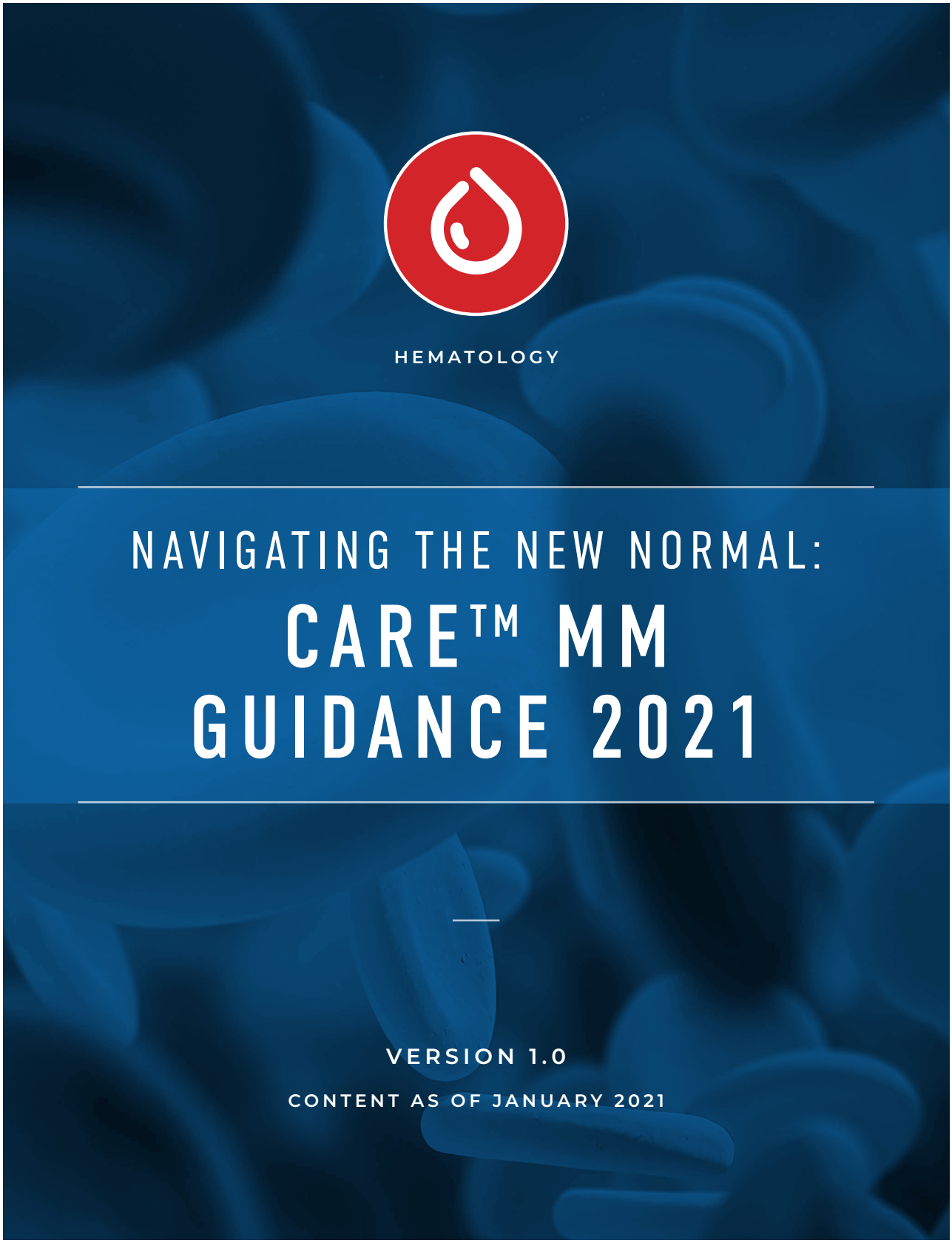

HEMATOLOGY

NAVIGATING THE NEW NORMAL:

CARE™ MM GUIDANCE 2021

VERSION 1.0

CONTENT AS OF JANUARY 2021

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A GUIDANCE FOR CLL HAS ALSO BEEN CREATED: CLICK HERE TO ACCESS

VERSION 1.0 - CONTENT AS OF JANUARY 2021

CARE™ MM GUIDANCE 2021: NAVIGATING THE NEW NORMAL

BACKGROUND

In July 2020, The CARE™ Hematology Faculty developed and published Considerations for Malignant Hematology Patient Management and Treatment During the COVID-19 Era.

Changes in the delivery of care brought on by the pandemic have happened fast, despite not necessarily being optimal for patient outcomes. These changes, as well as increased complexity with MM treatment decisions with availability of novel agents have prompted the CARE™ Faculty to create the CARE™ MM Treatment Guidance: Navigating the New Normal in 2021.

This is the 1st iteration (V.1) of the CARE™ MM Treatment Guidance. It aims to provide further context and guidance specifically on management of MM as clinicians navigate the new normal in 2021.

CONTENT PROVIDES UPDATES ON:

CARE™ Treatment Algorithms for frontline and relapsed/refractory (R/R) MM

- Suggested/available treatment options with additional information to consider when approaching patient care in today's landscape

Considerations Prior to Initiation of Therapy

- Pre-clinic/consult consideration during COVID-19
  - Consider whether consultation should be done in-clinic vs. virtually
  - Decisions for treatment initiation or continuation considers local infection rates and the risk to the patient of contracting COVID-19
- Defining High Risk Disease
  - Overlapping genetic abnormalities (including 1q gain) + ISS stage can fine-tune risk and better predict ultra-high risk, early relapsers

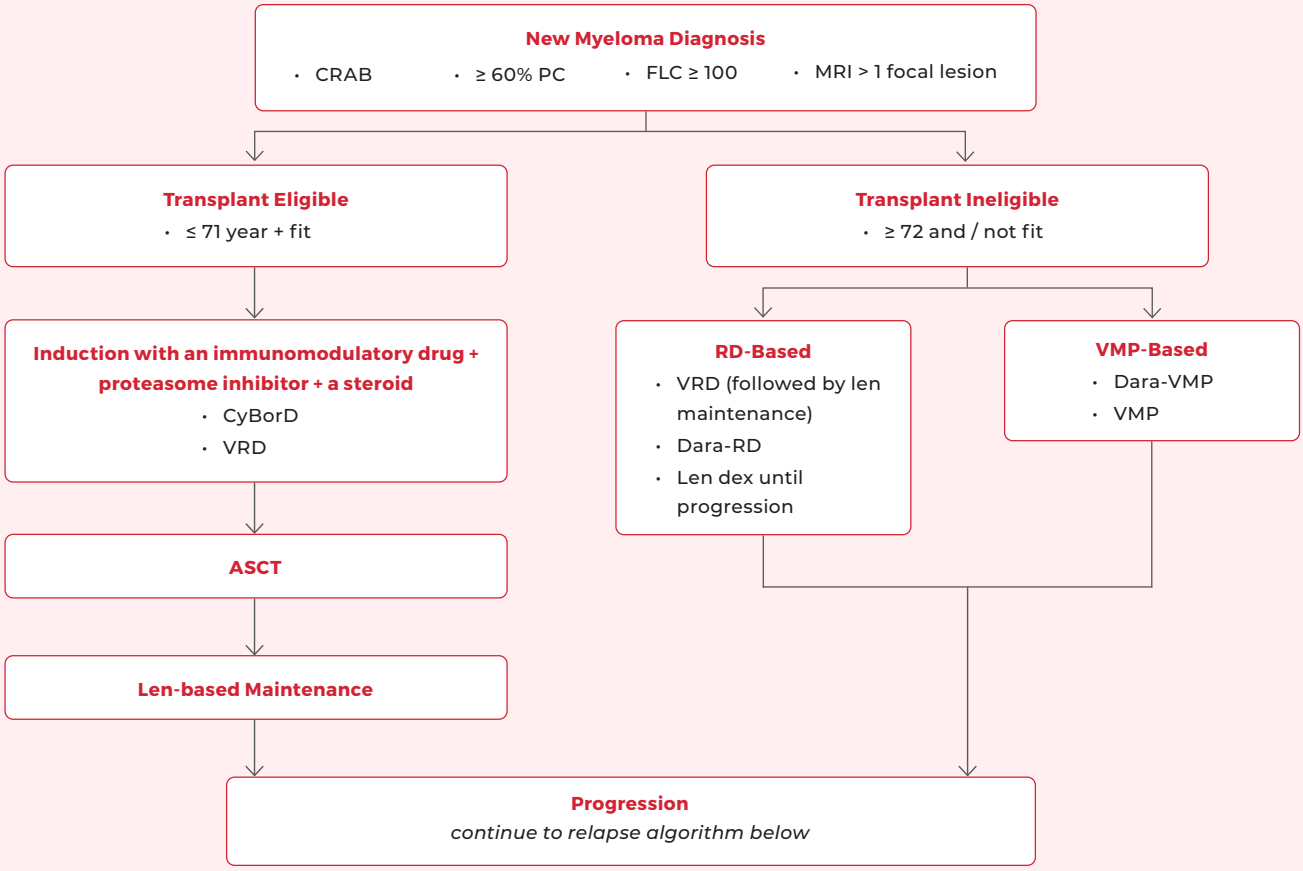
Considerations for Management of Patients During COVID-19

- Therapeutic decisions should remain to be based on individual factors
- Oral, and sub-cutaneous drugs reduce time and frequency of potential exposure so should be prioritized

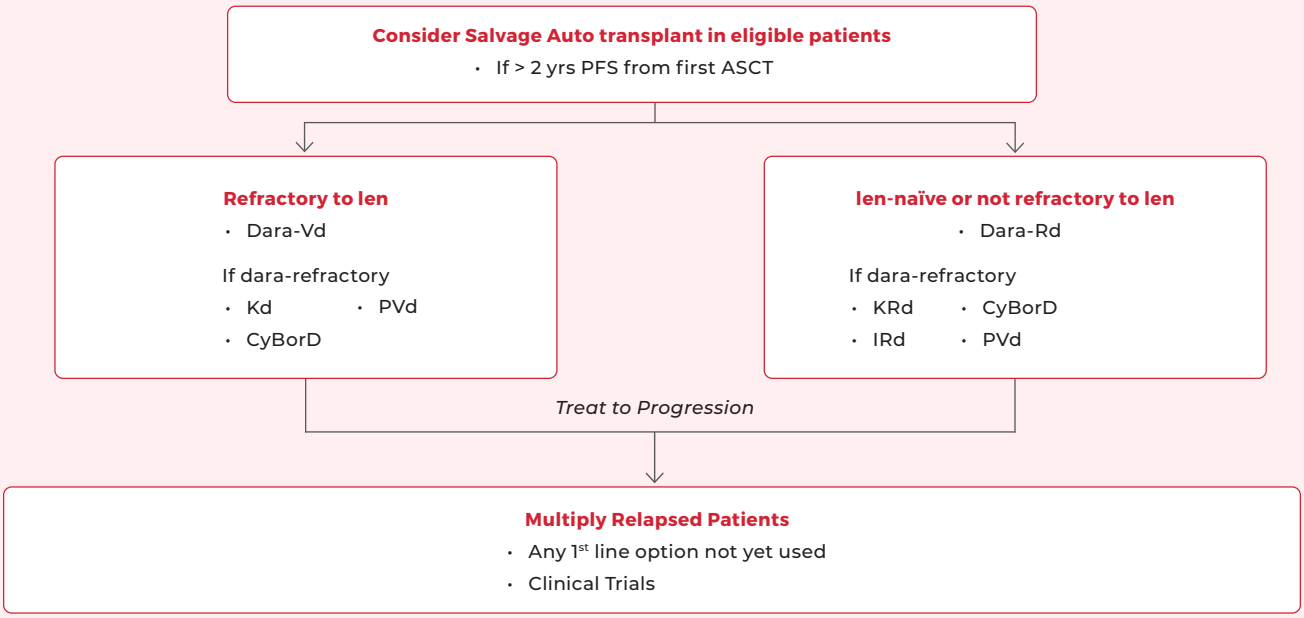
Moving Forward

- Focus moving forward will be on strategies that maximize magnitude and duration of response, and improve outcomes for difficult to treat patient populations (i.e. lenalidomide refractory patients)

FRONTLINE NDMM: NEWLY DIAGNOSED MM



RELAPSE (1-3 PRIOR LINES)



SUPPORTING INFORMATION/DISCUSSION

CONSIDERATIONS PRIOR TO INITIATION OF THERAPY

Pre-clinic/consult considerations during COVID-19

Assess whether an in-clinic visit is warranted: The decision between in-clinic vs. virtual consultations should be made on an individual patient basis considering factors, such as:

- COVID-19 infection rate in the respective community
- Stage of disease

If an in-clinic visit is warranted:

- **Share protocols with patients before coming to clinic** (masking of all patients, physical distancing, hand and surface hygiene, and identification of upper respiratory infection symptoms)
- If possible, organize investigative tests and face-to-face consultations so that the patient spends as little time as possible in the hospital
    - **Most centers will have a COVID-19 testing protocol appropriate for their circumstances in place**

Advance planning in case of telehealth or virtual consult:

- Obtain informed consent prior to the initiation of virtual care/telehealth
- If a choice of telehealth is the direction for consult – patient education material "how to access/use" should be provided

Initiate or Delay therapy?

Decisions for treatment initiation or continuation must:

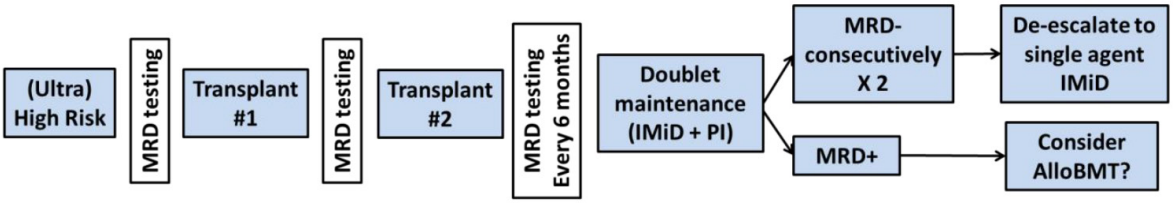
- Be considered for both uninfected patients and SARS-CoV2- positive patients if they are a- or paucisymptomatic
- Take into account local infection rates and risk to the patient of contracting COVID-19
- Be implemented after a proper risk/benefit explanation with the patient

In areas where COVID-19 is endemic, delaying starting therapy may be appropriate for smouldering, NDMM, and in relapse setting. However, watch and wait patients can feel anxiety that their MM will/is progressing while they are not on therapy. Patients with active or high-risk disease need treatment to avoid morbidity and mortality.

Defining High Risk Disease

High risk disease in MM refers to the group of patients who achieve suboptimal responses to therapy, early and aggressive relapses, and early death. Overlapping genetic abnormalities (including 1q gain) + ISS stage can fine-tune risk and better predict ultra-high risk, early relapsers (Kaiser et al. ASH 2019 Abstract 0604). **High risk disease remains the greatest area of unmet need in MM.**

Figure. Princess Margaret Protocol for Managing Ultra High-Risk Disease



CONSIDERATIONS FOR MM TREATMENT DURING COVID-19

- Therapeutic decisions should be made on a case-by-case basis, considering disease stage, risk, setting, cytogenetics/ FISH, age, comorbidities
- It is imperative that clinics ensure open and proactive communication with patients about COVID-19 protocols in place at clinic, how to maintain access to value clinic and support services, therapeutic options being considered, and any potential risks associated with their care during COVID-19
- Oral, and sub-cutaneous drugs reduce time and frequency of potential exposure so should be prioritized
  - Oral and weekly regimens are preferable to multiple trips to the clinic especially with those patients who have stable standard risk disease
  - The sub-cutaneous formulation of daratumumab is now approved in Canada (August 2020, based on Phase 3 COLUMBA study; Mateos et al. The Lancet, 2020) and can be administered in minutes vs. hours with IV
- The use of triplet regimens with the need for parenteral administration is dependent on local COVID concerns
- For young patients with newly diagnosed MM, ASCT may be delayed depending on local circumstances with increased number of induction cycles administered (i.e. 6-12 cycles of CyBorD or RVd) Dexamethasone use and dose may be reduced
- Maintenance therapy can be continued with oral therapies preferred and telemedicine utilized to lessen the number of clinic visits
- Unless there is a life-threatening situation, patients who exhibit infectious symptoms consistent with the pandemic should not be treated with chemotherapy (CCO 's Pandemic Planning Clinical Guidelines for Patients with Cancer)

MOVING FORWARD

Regarding Clinical Updates - novel regimens to watch for on the horizon include:

- Novel CAR T and BiTE approaches with immune novel targets are in early phase trials
- KDd – carfilzomib, daratumumab, dex (CANDOR, KDd versus Kd in patients with 1-3 prior LOT)
- SPd – selinexor, pomalidomide, dex (STOMP, investigating SPd in patient with 2-8 prior LOT)
- Ven-Bd – venetoclax, bortezomib, dex (BELLINI, Ven-Bd versus placebo - Bd in patients with 1-3 LOT)

Regarding COVID-19 - It is important that we continue to review clinical and real-world data as it becomes available, as well as consider how patient care will change with wider availability of COVID-19 vaccines.

As more patients begin to go back into clinic, anticipating and planning for challenges with patient load and testing delays will be necessary.

CARE™ HEMATOLOGY FACULTY

The CARE™ (Community. Academic. Research. Education) Faculty is a Pan-Canadian group of leaders in their field who gather, discuss and address gaps in knowledge, to develop education initiatives that frame news from a Canadian perspective.

The **vision** of the CARE™ Faculty is to share opinions and update Canadian specialists and allied healthcare providers with news and developments, framed from a Canadian perspective.

The **mission** of the CARE™ Faculty is to enhance medical education, with the explicit goal of improving patient outcomes.

Learn more at www.CAREeducation.ca

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