FAQS from Dr. Skikne's webinar

Question of adding Luspatercept to Procrit. This is being studied. It would be ideal if both could be administered - if insurance would approve. The first thing may be to increase the Procrit dose in each injection. If no response within 4 weeks, then try switch to luspatercept. If this fails, would then try to add lenalidomide - will be fine if both Procrit and lenalidomide are administered at the same time. GFR=39 indicates that likely his kidneys do not make adequate levels of erythropoietin to make adequate numbers of red blood cells. Ensure that he eats fresh fruit and salad at least a few times per week. If not, he should be on folic acid tablets - 5 mg per day if possible and should check the vitamin B12 level. A bone marrow is always helpful to tell if the disease is stable or progressing and I would do this between 3-6 monthly with such patients - despite their age.

Question on patient on luspatercept and now without transfusion requirement. When ferritin levels are that raised, they are not accurate in that 2965 and 2990 may be viewed as no different. There are reasons why they lose their accuracy that I could spend about a page on explaining. The ferritin level may very slowly decline over months. If hemoglobin goes up by 1 gm, you could expect the ferritin to go down by about 20, thus if Hb goes up by 2 g/dL, then expect ferritin to decline by about 40. Not very much. At this ferritin level, he should hopefully be on an iron chelator. To reduce the ferritin to reasonable levels with luspatercept alone will take some many months. Also, the ferritin levels in MDS can be higher than reflected by their body iron content due to a number of inflammatory proteins that cause the ferritin to rise besides body iron content.

Question on low platelet count and iron overload - Is this a concern? Ferritin of 900 is not severe iron overload, but if it keeps on rising and gets to as high as 1500, then chelation therapy is in order. Low platelets are a concern when it gets below 50,000 and especially if it is <25,000.

Question on alternate drug to cyclosporin as it can cause kidney dysfunction. if it is inducing a response, it may be that the dose can be slowly titered down to find if a lower dose can still lead to a response. Tacrolimis also can cause renal dysfunction. Other immunosuppressant drugs could be tried but they do not have not have a good track record or have not been studied.

Question from patient with TET2 and STAG2 mutation after chemo and radiation therapy. The optimum way to check for new mutations is by a bone marrow. We try to do this on our patients on a 3-6 month basis depending on their individual MDS situation. Mutations can be found on blood testing but this may not be as accurate and some insurance companies do not always pay on testing for mutations using blood testing.

Question on luspatercept and shortness of breath versus when had Aranesp. Luspatercept should not cause shortness of breath. If it is doing so, this is unusual. Question is why taking luspatercept if they were on Aranesp. Did Aranesp efficacy stop and that is why now on

luspatercept? If so, it is more likely that the disease is progressing and not responding to luspatercept. If the anemia is getting worse, then consider changing to another therapy.

Question on how much is known about the RUNX1 mutation. RUNX1 is not an unusual mutation in these malignancies and it is of interest that this has occurred at least in you and your 39 yr old son. And then you had a son with AML as well but as I understand was not identified to have RUNX1. It would be interesting to know if he also carried this gene abnormality and it is possible that if he had a transplant that the transplant center still has a vial of blood frozen away that could be tested for the RUNX1 mutation. One can sometimes work out if the mutation runs in families - known as a germline mutation or if this was an acquired mutation by looking at the variable allele frequency - is the abnormality present in around 50% of the RUNX1 genes and one can test to see if this mutation can be found in cells that are not made in the bone marrow such as from the skin or oral lining cells. This may help better understand why you and 2 children have diseases in which this mutation is involved. This mutation can sometimes indicate that the disease may behave more aggressively - if it was not a germline mutation - runs in families.

Low platelet count question around 30,000. You should not bleed spontaneously with this platelet count but avoid any form of trauma or injury and if you need surgery, you may need a platelet transfusion. Do not take aspirin or NSAIDS - ibuprofen, Advil, Aleve as these can make you bleed more. Treatment may include hypomethylators - Vidaza or Dacogen or thrombopoietin mimetics such as Romiplostin or eltrombopag. Occasionally, androgen treatment can help and is worth trying for about 3 months.

What is median prognosis of high risk MDS? This is about 3.5 yrs but range is from about 8 months to up to 5 yrs. Thus if possible to obtain we recommend a bone marrow transplant, but hypomethylator therapies such as Vidaza and Dacogen can prolong survival and we would definitely try these agents.

My husband has del(5q) and anemia. Definitely start with Procrit or Aranesp but at higher doses. If there is no response by 6 weeks the dose should be increased. If no response with this, one can try adding G-CSF (Neupogen) to the Procrit or abandon this and start Revlimid which usually works in about 60% of cases and 85% of responders have the response in the first 4 cycles of therapy.

Upper limit of number of transfusions that patients can receive? There is no upper limit to the number of transfusions that one can have but, the big issue is development of significant iron overload after about 12 units of red blood cells and if ferritin is greater than 1000, that is a good guide to starting an iron chelator treatment. There are other side effects of getting blood transfusions but iron overload is the most concerning.

My 89 year old father was diagnosed in 2009. Once AML occurs, are there viable treatment options? If transformation to AML occurs, it is treatable usually with Vidaza or Dacogen. I do have MDS patients whose MDS has transformed to AML and they do extremely well with

these agents – I prefer Vidaza. However, should they already been treated with either of these agents and then AML occurs, this is more difficult to treat – but, there are certainly experimental agents to try and review gene mutations that may be present that sometimes help one to decide on what therapy to use.

Prognosis of unclassified MDS/MPN. This depends on the blood counts, cytogenetics and gene mutations. The overlap of these two disorders does not necessarily connate that the prognosis is any worse than if one had MDS only or MPN only.

Lowest HgB level before transfusion must be given? Generally, this is less than 7 G/dL. However, if one has heart or lung disorders, this should be 8 G/dL. However, I prefer to transfuse if the HgB is below 8 and most studies use HgB of 9. Some patients can tolerate HgB levels as low as 5 but in older persons, I do not want the HgB to be <7.

Prognosis of patient requiring weekly transfusions. One should always check that bleeding is not producing this need for blood and sometimes there could be excess destruction of red blood cells occurring due to antibodies destroying the red blood cells.

Normal range of band/segmented neutrophils? Look at the absolute count. If below 1.8/uL this is low. Below 0.5 it is very low.

Is occasional pain in leg bones related to MDS? Pain can occur because of expansion of the bone marrow growing in these bones, but this is uncommon.

What is the age cut off for stem cell transplant? In the USA, it is 75 yrs.