Welcome to the Yale Ash 2021 highlights.

My name is Bob Bone. I’m one of the hematologist at Yale, and I’m happy to facilitate this session today.

As we are focusing on some of the important abstracts from the previous Ash meeting relating to classical hematology.

And today we have 3 presenters who will each present abstracts for about 15 minutes. We’ll take questions at the end of the session and they should be entered into the chat room or to the Q&A.
Before we start, let me take a moment to introduce our presenters. First Kelsey Martin, who is an assistant professor in clinical medicine at the Yale School of Medicine, and she practices hematology oncology at the Orange Care Center and has a special interest in classical hematology, and particularly the intersection of obstetrical care and hematology. Doctor Sudhanshu Mulay who is the medical director of the anticoagulation clinic at Saint Francis Hospital and Medical Center and he also has a strong interest in classical hematology and transfusion medicine.
He's an assistant professor of medicine at the University of Connecticut. And then finally Doctor Alex Pine, who's assistant professor of medicine and hematology at the VA Medical Center. He and his colleagues have done significant work over the past few years, detailing the mechanisms of COVID Coagulopathy. So without further ado, I'll introduce Doctor Martin and let her begin the presentations. Great, thank you so much. Good afternoon everyone. Is my volume OK? Correct, alright.
I’m going to be discussing A3 abstracts relating to bleeding disorders. First, abstract is titled efficacy and safety of the two Serin prophylaxis, a small molecule RNA interference therapeutic in a multicenter phase. Three study called Atlas I NH in people with hemophilia A or B with inhibitors. This was presented at the plenary scientific session by Doctor Gayoung from University of Southern California. 1st, I’ll provide some background. Hemophilia A&B are rare bleeding disorders that are characterized by ineffective clot formation, largely due to impaired thrombin generation.
As a result of severe deficiency of factor 8 and 9, currently our standard of care largely relies on replacing the missing factor. There is a high rate of development of anti factor inhibitors which is up to about 30% in some of our patients with hemophilia A and about 5% of the patients with hemophilia B. Subcutaneous fat isran is a novel therapeutic. It's a small molecule RNA interference therapeutic that acts by binding and degrading at the M RNA which encodes for antithrombin.
thereby partially silencing the expression of antithrombin.

This rebalances hemostasis and restores thrombin generation in patients with hemophilia or A and has been demonstrated to be effective in patients with or without inhibitors as I'll discuss.

This study demonstrated that prophylactic use of the two strands significantly reduced annualized bleeding rates, which is essentially bleeding events on an annual basis in patients with hemophilia A or hemophilia B that have inhibitors,
and demonstrated both efficacy and safety data.

In this study, 57 patients were randomized, 2 to 1 in an open label phase. Three trial patients were males over the age of 12, again with either hemophilia A or B, and these were patients that had been receiving on demand treatment with bypassing agents for Blake breakthrough bleeding. There was 38 patients in the phase, two Syrian group and the dosing of this medic.
This is a subcutaneous therapy that was given at 80 milligrams once a month versus 19 patients in the on demand bypassing Agent Group. They were followed. The primary endpoint was looking at annual bleeding rate in the efficacy period, which was nine months. Secondary endpoints looked at spontaneous bleeding rates, joints, bleeds, quality of life metrics, and frequency of the bleeding episodes that happened in the onset period, which was the first month of therapy as
well as safety and tolerability data. And this was demonstrated to be extremely effective in the future and patients. So you can see here on this first line the median annual annualized bleeding rate was actually 0. The estimated rate was 1.7 versus in the bypassing agent group. The median annualized bleeding rate was 16.8. And there was actually the median for spontaneous bleeds with zero in the future and category. There was also demonstration of significant quality of life.
improvements based on the validated quality of life screening tool.

And it was effective in both patients with hemophilia A and in patients with hemophilia B.

And we can see that 29 patients received a two-strand agent only with a very significant P value.

Overall, the agent was well tolerated.
although the main side effect of special interest was thrombotic events. Uhm? There was no deaths of any kind in either group of note. Of the patients that had thrombotic events, the authors reported that that occurred in some patients that seemed to have the antithrombin levels at the lower end of the range and seen some as low as 10 to 20%, and which is what they attributed to and only one patient who had a thrombotic event ended up coming off study, and this was a patient who had a thrombosis in a spinal vein.
Other side effects were increases in transaminases, but the authors reported that this did not impact any of the treatment scheduling, and no patients had to come off trial for any changes in hepatic enzyme changes. So the conclusions were that the two Serin had significant improvements in the treatment arm compared with the on demand bypassing agents. And this is seen as somewhat of a game changer in the sense that it’s a tremendous change in practice where patients are given monthly and subcutaneous, compared to the current standard of practice where patients are
NOTE Confidence: 0.970921658
00:07:35.180 --> 00:07:36.940 needing intravenous therapies and.
NOTE Confidence: 0.970921658
00:07:36.940 --> 00:07:40.050 In a much higher frequency.
NOTE Confidence: 0.970921658
00:07:40.050 --> 00:07:42.269 Nearly 2/3 of the patients treated with
NOTE Confidence: 0.970921658
00:07:42.269 --> 00:07:44.390 fattoush Rand had zero treated bleeds,
NOTE Confidence: 0.970921658
00:07:44.390 --> 00:07:46.355 and the mean median annualized
NOTE Confidence: 0.970921658
00:07:46.355 --> 00:07:47.927 bleeding rate was zero.
NOTE Confidence: 0.970921658
00:07:47.930 --> 00:07:48.920 And of note,
NOTE Confidence: 0.970921658
00:07:48.920 --> 00:07:50.900 this is also efficacious in both
NOTE Confidence: 0.970921658
00:07:50.900 --> 00:07:52.890 patients with hemophilia and hemophilia
NOTE Confidence: 0.970921658
00:07:52.890 --> 00:07:55.278 B and its patients with hemophilia
NOTE Confidence: 0.970921658
00:07:55.339 --> 00:07:57.326 B have really had not had similar
NOTE Confidence: 0.970921658
00:07:57.326 --> 00:07:58.694 prophylactic similar prophylactic
NOTE Confidence: 0.970921658
00:07:58.694 --> 00:08:01.430 options as our hemophilia A patients.
NOTE Confidence: 0.970921658
00:08:01.430 --> 00:08:05.382 So creating a new sort of treatment
NOTE Confidence: 0.970921658
00:08:05.382 --> 00:08:07.265 approach 7 patients in the treatment
NOTE Confidence: 0.970921658

13
arm had at least one adverse event, including.
The four thrombotic events and one of those patients did require withdrawal from this study.
That concludes my discussion in the first abstract, and I'll move on to the second.
The second abstract was titled rate of prolonged response after stopping THROMBOPOIETIN receptor agonist treatment in primary immune thrombocytopenia results from a nationwide prospective multicenter interventional study. And this was out of France.
Some background information.

There’s been several retrospective studies and a recent prospective study that reported unexpected cases of durable remission after TPO receptor agonist were discontinued in adult patients with ITP. This has been seen in up to 30% of these patients. However, it felt that perhaps some of the newly diagnosed ITP cases in which spontaneous remissions occurred may have been included in most of these studies. So the question this study has is what
00:09:14.838 --> 00:09:16.959 proportion of patients with either
NOTE Confidence: 0.90684127
00:09:16.959 --> 00:09:20.036 persistent or chronic phase ITP and no
NOTE Confidence: 0.90684127
00:09:20.036 --> 00:09:22.574 recent exposure to any potentially curative
NOTE Confidence: 0.90684127
00:09:22.574 --> 00:09:25.369 therapy such as splenectomy or rituximab,
NOTE Confidence: 0.90684127
00:09:25.370 --> 00:09:28.172 achieve a long term remission off
NOTE Confidence: 0.90684127
00:09:28.172 --> 00:09:31.238 treatment at 24 weeks and 52 weeks.
NOTE Confidence: 0.90684127
00:09:31.240 --> 00:09:33.347 After having on at least three months
NOTE Confidence: 0.90684127
00:09:33.347 --> 00:09:35.879 of their TPO receptor agonist exposure,
NOTE Confidence: 0.90684127
00:09:35.880 --> 00:09:39.441 who had a complete response
NOTE Confidence: 0.90684127
00:09:38.400 --> 00:09:39.441 and persistent phase,
NOTE Confidence: 0.90684127
00:09:39.441 --> 00:09:41.870 ITP is is defined as those with
NOTE Confidence: 0.90684127
00:09:41.943 --> 00:09:43.779 ITP between 3 and 12 months,
NOTE Confidence: 0.90684127
00:09:43.780 --> 00:09:48.456 whereas chronic phases lasting for beyond 12.
NOTE Confidence: 0.90684127
00:09:48.460 --> 00:09:50.590 Months, so the inclusion criteria.
NOTE Confidence: 0.90684127
00:09:50.590 --> 00:09:53.355 So again, this was a nationwide prospective
NOTE Confidence: 0.90684127
00:09:53.355 --> 00:09:54.540 multicenter interventional study.
The inclusion criteria included patients over the age of 18 with either persistent or chronic primary ITP. They needed to have a stable complete response, which was defined as a platelet count of more than 100,000 for more than two months on their TPO RA therapy and they needed to have been on treatment with their TPO RA for at least three months. Exclusion criteria was patients who are on either anticoagulation or antiplatelet therapy. A patient who had previously failed the treatment...
TPRA agent and the patient could not have been receiving any concomitant steroid or cortico steroid or IVIG, and they could not have had Rituxan mab, nor splenectomy within either the two months preceding or after initiation of their TPO or RA therapy. And the patients underwent a progressive dose reduction and they had to. There are TPO therapy or a therapy had to be stopped by 10 weeks and they proposed a method whether it was a Rama, Plasty, Morrell, Trumbo bag of a protocol of how to how taper off their doses accordingly. And if a patient relapsed during
after this discontinuation, the decision to start a new therapy was left at every investigators discretion, and so the primary endpoint was what was the proportion of patients who achieved an overall response, which was defined as CR plus R at week 20 at week 24. So six months afterwards, and the secondary outcomes looked at those, the overall response rate after a year or 52 weeks, they look. I didn’t looked at patients who had bleeding events, and they aimed to try to identify
any predictive factors to see which patients might be those who achieve. Such an overall prolonged response. So 49 patients which included a 30 females with either persistent. There was an end of two or chronic and a 47 ITP. The median age of 58.5 years were evaluated in this two year period over 22 centers. 40 of the patients had received eltrombopag and nine around the plastic. And intention to treat analysis. 56.2% so 27 of the 48 patients achieving the primary endpoint and maintained an overall response at 24
weeks after TPO RA discontinuation.

And of those, half of those,

essentially 55 percent, 15 of those,

which again is defined as a

platelet count over 100,000.

Bleeding events did occur in 61.9% of

the patients and 65.2% of the patients

who did relapse at the 24 week and 50.

Should be weeks or 52 weeks with the median

platelet count of 31,000 at that time.

No severe bleeding episodes occurred.

And they could not identify any

predictive factors. Neither age.

Which agent the patient had,
how long they’d had. None of these things were able to predict which patients were those who were going to achieve such a sustained response. So the conclusions of this was that after 52 weeks and this is you can see by the diagram on the right hand side after TPR, a discontinuation overall response was seen in about half of these patients, 52.1% for those who did relapse. The median time of relapsing after tapering was at about 8 weeks, but the majority of those actually happened within the first two weeks.
and none of those patients who relapsed developed severe bleeding.

In among 21 patients who did relapse before week 2413, of those were able to be re challenged with their TPO RA and they were still able to achieve a complete response with a medium time of two weeks.

So the conclusion is that there was a high rate of sustained off treatment remission after TPO RA discontinuation in patients with chronic ITP who had initially achieved at stable CR. They were unable to die and identify a predictive factor of which patients were
00:14:03.345 --> 00:14:05.850 would achieve such a lasting remission.
NOTE Confidence: 0.871721324333333
00:14:05.850 --> 00:14:07.806 But this study strongly supports use
NOTE Confidence: 0.871721324333333
00:14:07.806 --> 00:14:09.849 of a progressive tapering off of the
do TPRS and patients who do
NOTE Confidence: 0.871721324333333
00:14:09.849 --> 00:14:11.431 achieve a stable CR on treatment.
NOTE Confidence: 0.871721324333333
00:14:11.490 --> 00:14:13.230 And there may be opportunity for us
NOTE Confidence: 0.871721324333333
00:14:13.230 --> 00:14:16.131 to be able to discontinue therapy
NOTE Confidence: 0.871721324333333
00:14:16.131 --> 00:14:16.995 in such patients.
NOTE Confidence: 0.820428353333333
00:14:20.790 --> 00:14:22.660 The last abstract I'll discuss
NOTE Confidence: 0.820428353333333
00:14:22.660 --> 00:14:24.156 was called obstetric obstetrical
NOTE Confidence: 0.820428353333333
00:14:24.156 --> 00:14:25.910 and perioperative management of
NOTE Confidence: 0.820428353333333
00:14:25.910 --> 00:14:28.110 patients with factor 11 deficiency.
NOTE Confidence: 0.820428353333333
00:14:28.110 --> 00:14:30.258 A retrospective observational study.
NOTE Confidence: 0.831983915625
00:14:32.860 --> 00:14:34.772 In the background information
NOTE Confidence: 0.831983915625
00:14:34.772 --> 00:14:36.684 data regarding obstetrical and
NOTE Confidence: 0.831983915625
00:14:36.684 --> 00:14:38.024 perioperative management of
factor 11 deficiency is scarce.

And the question at hand is, can we create a database of such patients and identify factors associated with increased bleeding risk in patients with factor 11 deficiency during childbirth or surgery? And this was presented by Doctor Hanna from the Icahn School of Medicine at Mount Sinai.

So they did a retrospective chart review of patients with factor 11 deficiency who underwent either childbirth or surgical procedures over a 10 year period within the Mount Sinai.
health care system in New York City, and they collected data on age, sex, ethnicity, genotype, family history, personal history of bleeding. The type of anesthesia used the estimated blood loss and any evidence of periprocedural bleeding which patients needed blood product administration and which product which patients needed hemostatic agents in the perioperative period, they defined a bleeding endpoint as acute postpartum or post operative hemorrhage, any bleeding that warranted non prophylactic administration of pack red blood cells.
FFP or tranexamic acid.

They performed a logistic regression to test for the association between either historical, laboratory and procedural variables with the bleeding endpoint.

So overall, 198 patients were evaluated who had undergone 252 procedures in total. This included 143 vaginal deliveries in 64 city sections and 45 other surgical procedures.

38 of the 252 procedures did result in bleeding complications, and they found that both a prior history of bleeding and a lower
factor 11 levels were independently associated with the bleeding endpoint. Interestingly, 8 out of 21 patients, 38% who suffered a bleeding complication. This happened despite prophylactic FFP. The mean factor level level for patients who receive neuraxial anesthesia was 50 units per deciliter. In five patients with a negative bleeding history, despite surgical challenges, we’re actually able to receive neuraxial anesthesia effector level levels less than 10 and without any bleeding complications, and only one of these had
00:16:59.342 --> 00:17:00.383 received prophylactic FFP.

00:17:05.260 --> 00:17:07.458 So their conclusions were that a personal history of bleeding was the strongest predictor of perioperative or obstetrical bleeding and that personal history of bleeding was actually defined as just one report of heavy menstrual period or bleeding in the operative period.

00:17:11.426 --> 00:17:13.817 It just took sort of one event in time to define a personal history of bleeding factor.

00:17:13.817 --> 00:17:15.974 11 levels were found to correlate with a slightly slightly lower but statistically significant odds of surgical bleeding, and they found that a factor

00:17:20.040 --> 00:17:23.068 It just took sort of one event in time to define a personal history of bleeding factor.

00:17:23.068 --> 00:17:25.504 define a personal history of bleeding factor.

00:17:27.936 --> 00:17:29.973 slightly lower but statistically significant odds of surgical bleeding,
deciliter may predict bleeding risk.

With reasonable specificity at 83% but lacked sensitivity,

they also found that factor 11 levels are stable during pregnancy,

as demonstrated by the diagram on the bottom right,

showing that repeat measurements may not be necessary,

which is something commonly done in practice,

and they also found that neuraxial anesthesia appeared to be safe to use in this cohort,

which clinically is a question

that comes up frequently.

Hey, thank you for your time.

Forward to hearing from our next speaker,
Doctor Malik.

Thanks, Kelsey.

Right, thank you for the opportunity to talk today.

I’m going to focus on thrombosis, so I’m hoping to present three studies that I found of interest.

Have one focus study and then as time permits and go through the other two studies with quickly.

The focus state I would I would like to present is 1 listed here by Murs ET al from the Brigham.

and Women’s Hospital in Boston who looked at anticoagulation use and
outcomes among patients with atrial fibrillation and vanilla brand disease.
The background is that estimated prevalence of symptomatic 1 willbrand disease is about one in 1000. It is estimated that
Patients with one milligram disease have similar prevalence of atrial fibrillation as general population is about .84%.
The American College of Cardiology recommends using anticoagulation for those with atrial fibrillation who have chads, vascor of two or greater in men or three or greater in women.
The recent ISTH-NHF guidelines recommend using anticoagulation or antiplatelet therapy as clinically indicated. It was a suggestion with low certainty of evidence and importantly when I looked into the actual basis of this recommendation, it was based on a case series of about 60 patients or really low quality data. So this the study that was presented was a retrospective study in which data was obtained from the Electronic medical records. Patient was selected if they had a diagnosis of 1 lip and disease.
00:20:27.117 --> 00:20:29.067 noticed or seeking cofactor activity
00:20:29.067 --> 00:20:31.896 or any abnormal one will event factor
00:20:31.900 --> 00:20:34.582 measurements and also selected for those
00:20:34.582 --> 00:20:37.910 who had diagnosis of atrial fibrillation.
00:20:37.910 --> 00:20:40.381 The primary endpoint was rate of major
00:20:40.381 --> 00:20:42.730 bleeding as defined by the IST criteria,
00:20:42.730 --> 00:20:44.038 which is fatal.
00:20:44.038 --> 00:20:45.782 Bleeding, bleeding in critical
00:20:45.782 --> 00:20:47.828 organs or bleeding causing more
00:20:47.828 --> 00:20:50.810 than two grams of two grams per DL,
00:20:50.810 --> 00:20:53.510 drop in hemoglobin or more than two
00:20:53.510 --> 00:20:54.950 units of red blood cell transfusion.
00:20:54.950 --> 00:20:58.078 Sorry with the typo.
00:20:58.080 --> 00:21:02.274 The results were that patients in
00:21:02.274 --> 00:21:04.730 tribulation patients were between
diagnosed between 1980 and 2020.

89 patients were selected.

Out of those 64 patients were female,

28% patients were deceased at the time of the data pool.

Medium Chance Best Score was three and 89, so close to 90% had a score of two or higher.

A third of the patients also had a quote acute coronary syndrome, which the authors lumped together as STEMI non STEMI and Angela.

In the in the figure over here as we can see,
About 13.4% of the patients were ever prescribed P2Y2 inhibitors and 56.2% were ever prescribed an anticoagulant. The green color represents people with antiplatelet agents who also had a diagnosis of acute coronary syndrome. About 1/4 of the patients were never prescribed any anticoagulant or antiplatelet agent. In these two graphs we can see the median time to 1st bleeding event on the left we have antiplatelet agents and on the right it's...
anticoagulants as we can see in both. It looked like the median or the time taken for median first meeting was greater than 15 years. For both of these study groups.

Just going into the raw numbers, 10.2 events per hundred patient years. So the rate of major bleeding was 10.2 events per hundred patient years. For those on platelet agents, 8.9 events per hundred person years. For those on anticoagulants without any statistical difference between the two groups.

Baseline risk of bleeding was one event per hundred patient years,
00:23:14.660 --> 00:23:17.264 so these were the patients who
00:23:17.264 --> 00:23:19.000 never got antiplatelet therapy
00:23:19.071 --> 00:23:20.850 or anticoagulant therapy.
00:23:20.850 --> 00:23:22.218 Concomitant anticoagulant and
00:23:22.218 --> 00:23:24.042 antiplatelet agents resulted in
00:23:24.042 --> 00:23:26.179 much higher risk of bleeding,
00:23:26.180 --> 00:23:28.495 which was about 28 events
00:23:28.495 --> 00:23:30.347 per hundred patient years.
00:23:30.350 --> 00:23:33.157 The lifetime risk of major beating was
00:23:33.157 --> 00:23:35.168 also calculated by the investigators,
00:23:35.168 --> 00:23:38.794 which was 32% in those who were
00:23:38.800 --> 00:23:41.158 ever prescribed anticoagulants,
00:23:41.158 --> 00:23:43.978 and 25.6% who were never
00:23:43.978 --> 00:23:44.810 prescribed anticoagulants,
00:23:44.810 --> 00:23:46.845 and there was no statistical
difference between the two groups.

Looking at the stroke risk, the incidence of stroke was about 15.7%. And notably, 11 out of the 14 patients had never used and equivalent for more than not been prescribed anticoagulant for 90 days or more. The median chance best score was three in those who had stroke. And also those who are not anti-quietly therapy. One of those patients who had a stroke had a fatal stroke. So the authors concluded that 50% of the patients in their study group.
were ever prescribed anticoagulant. There was no benefit in choosing antiplatelet therapy or anticoagulant therapy if bleeding rate is taken into account. There was no difference in lifetime risk of bleeding in those who were prescribed anticoagulants versus those who were not prescribed anticoagulants. Limited use of anticoagulant and antiplatelet therapy has much higher risk of bleeding, which is not surprising and 57% of patients had thromboembolic strokes. Most of those who were not therapy. So my take away from this study was that it was one of the largest
studies looking specifically at this population of one will appendices. Individuals who also have April fibrillation. It was a retrospective study, so has its own limitations, but it still provides one of the largest studies or largest evidence, which makes us probably feel a little bit more comfortable using anticoagulant in these patients with appropriate risk. Assessment of bleeding. Oftentimes antiplatelet agents are prescribed over antique violence as a way to reduce the risk of bleeding, but this study sort of makes us doubt that assumption.
00:25:48.480 --> 00:25:50.580 Details of 1 milligram disease subtypes were missing, and as we know, the severity of lung disease or the type of disease could make a difference to the bleeding risk. We also have noted recently that ristocetin cofactor activity may not be appropriate to diagnose patients with type 2 blip and disease, so some of those individuals were typed as one group and disease back in the previous years may actually not have one web and disease. Similarly,
practice patterns for A-fib management
as well as the choice of anticoagulation
has changed quite a bit since 1980s,
so that would certainly people founder.
We're gonna move on to the next.

So this was a man and also an
oral presentation.
Presented on behalf of Doctor Connors.

It was it was a meta analysis of
direct oral anticoagulants versus low
molecular weight heparin for treatment
of cancer associated thrombus.
In the in this study, the authors
looked at 6 randomized control trials.
The. This was an update to
the previous meta analysis,
which had four of these trials mentioned over here. The top four. So the two bottom ones were included in this meta analysis, so there were a total of 3690 patients out of which 1850 got direct oral anticoagulants and 1840 got local. The authors looked at the risk of recurrent venous from embolism, and it favored use of direct oral anticoagulants.

Incidence rate of recurrent VTE was 5.5%. In the electrolytic group and eight point 3% in the low molecular Weight Heparin group.
With the risk ratio of .67 favoring director.

Risk of major bleeding was about the same in the two groups,

so the incidence was four point 3% in the direct oral anticoagulants group and three point 7% in the low molecular weight Heparin group.

And statistically, there was no difference between the two groups.

The clinically non major bleeding.

Favored use of heparin,

so it was the incidence was 9.5% of this bleeding in the direct or anticoagulant group and five point 7% in the low molecular weight heparin group.
The risk was 1.6 and statistically favoring low molecular weight heparin group.

All 'cause mortality was similar in the two groups.

The conclusions drawn from this study of from this paralysis for that to act significantly reduce the risk of recurrent VTE compared with heparin, without increasing the risk of major bleeding.

However, use of direct oral anticoagulants was associated with increased risk of clinically relevant non major bleeding.

Finally, the last oral study that I
would like to present was about impact of race and ethnicity on cancer, associated thrombosis among underserved patients with cancer. This was an oral presentation presented by Doctor Decosta.

In this study, a retrospective analysis was done and the investigators identified 9353 patients. After those, 49.3% were Hispanics, 27.6% were non Hispanic blacks, 27.6% were non Hispanic whites and 7.6% were passed. Interestingly, 74.7% were uninsured, and the reason for this was the
study was primarily focused on a safety net hospital in Houston, which has this demographic of population. The incidence of cancer associated thrombosis was seven point, at six months and 9.6% at 12 months. Of previous studies which were primarily focused on Caucasian population, the risk at 12 months is much lower, about 2.3%. So something to keep in mind. On the graph on the left, we can see, as expected,
pancreatic upper GI where the OR
NOTE Confidence: 0.823889203333333
patients with pancreatic or upper GI
NOTE Confidence: 0.823889203333333
cancers were the ones with highest
NOTE Confidence: 0.823889203333333
risk of cancer associated thrombosis.
NOTE Confidence: 0.823889203333333
The interesting part was the top.
NOTE Confidence: 0.823889203333333
Sorry, the bottom right figure where
NOTE Confidence: 0.823889203333333
we can see that non Hispanic black
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population and non Hispanic white
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population seem to have similar
NOTE Confidence: 0.823889203333333
cumulative incidence of cancer
NOTE Confidence: 0.823889203333333
associated thrombosis at 12 months.
NOTE Confidence: 0.823889203333333
While Hispanic population and Asian
NOTE Confidence: 0.823889203333333
population seem to have a lower risk,
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so this contradicts what we have
NOTE Confidence: 0.823889203333333
traditionally known about thrombosis,
NOTE Confidence: 0.823889203333333
which is reported to be higher in
individuals with black ancestry.

And Hispanic population have been traditionally known to have a lower risk of thrombosis, so that is congruent with that knowledge.

When the authors did the multivariable analysis, they again found Hispanic race and Asian race were to have an impact on the risk of getting associated thrombosis.

The conclusions drawn were higher incidence of cancer. Associated thrombosis was noted compared to the European registries.
Non Hispanic blacks had similar incidence of cancer associated thrombosis to non Hispanic whites. Hispanic and Asian Pacific Islanders had a lower risk of cancer associated thrombosis compared to non Hispanic whites and non Hispanic black population. And treatment with chemotherapy or immunotherapy was associated with increased risk of thrombosis. That concludes my talk.
Alright, I’m so let me just start moving.

OK so hello buddy and Alex Pine and I wanted to briefly everybody on 3 potentially 4 abstracts. If we have time and. The first three are sort of have this ITP flavor and a couple of them has kovid color, so the first one is actually the first two kind of have the same motif, and they both studies actually looked into.

What happens to patients with persisting thermoset opinion when they receive COVID that vaccines and so the first study?
Which was out of Cornell.

Essentially they were operating on the premise that play, let's play play quite a bit of a role in immune immune system.

And also in their cohort, different cohort but in their center thrust opinion happened in 27% of patients with just COVID-19, so they. Actually postulated, or at least developed the concept further.

That in COVID-19, especially severe COVID-19, there's a a. This is normal glycosylation of the spike protein antibodies is a prothrombotic signal for platelets,
especially through.

Direct receptor these complexes of IgG and virus operate through the Cy come receptor and So what they? They also. There was also a clinical sort of observation.

Then there were some reports of ITP in post vaccine settings in a single institution. There was a 52 patients and there were 12% of ITP dissertations. So they asked the question. Several questions is in fact what is the effect of vaccines on platelet count, risk of bleeding events?
What kind of effect is in repeat dosing of vaccines? You know the second vaccine booster and so on, and what the risks of the actual exacerbation. What sort of plays a role in exacerbating so their cohort was retrospective from patients university affiliated patients that we actually also participated. It’s 117 patients. With a pretty long history of ITP 12 years. And of course they were.
the patients were getting vaccinated
were older patients.
So breakdown of what therapies were administered,
either on therapy or off therapy
So TPO, RA’s and we talk smack word
bulk of the the treatments,
and colectomy was also in 21% of
patients and at the time of the study 40 patients were off treatment and 16 of those were with normal platelet count.
This is a breakdown of.
00:36:38.830 --> 00:36:42.898 See the exchange that we received.

NOTE Confidence: 0.438028055

00:36:42.900 --> 00:36:45.015 Simon, of course majority and

NOTE Confidence: 0.438028055

00:36:45.015 --> 00:36:47.130 then definitions how they sort

NOTE Confidence: 0.438028055

00:36:47.210 --> 00:36:49.400 of were assessing the response.

NOTE Confidence: 0.438028055

00:36:49.400 --> 00:36:51.302 So stable platelet count was plus

NOTE Confidence: 0.438028055

00:36:51.302 --> 00:36:53.460 minus 20% of the pre vaccine level,

NOTE Confidence: 0.438028055

00:36:53.460 --> 00:37:01.090 and ITP exasperation was defined as either.

NOTE Confidence: 0.438028055

00:37:01.090 --> 00:37:03.526 Much higher than 50% reduction of

NOTE Confidence: 0.438028055

00:37:03.526 --> 00:37:07.702 platelet count or 20% reduction if you.

NOTE Confidence: 0.438028055

00:37:07.702 --> 00:37:10.198 If the if the native platelets

NOTE Confidence: 0.438028055

00:37:10.198 --> 00:37:13.159 below 30,000 or the use of rescue

NOTE Confidence: 0.438028055

00:37:13.159 --> 00:37:15.604 treatment and So what?

NOTE Confidence: 0.438028055

00:37:15.604 --> 00:37:18.181 They found that there’s a

NOTE Confidence: 0.438028055

00:37:18.181 --> 00:37:23.209 three groups of patients.

NOTE Confidence: 0.438028055

00:37:23.210 --> 00:37:26.586 I would say third or close to third
quarter places actually increased
platelet count increased in.
Happened in middle part like a 40%.
Nothing happened and in
about third so to speak,
it’s actually decreased and this is
the first Test of the second dose.
Sort of similar and they pointed out
that it may not be the same patience.
So they broke it down into
into several groups.
Specifically,
so they assessed all patients in
terms of incidence of post vaccine
ITP reservation splenectomy patients,
patients with me in patients with very heavily pretreated with five more than five, and more prior therapies, and so, interestingly enough, if you look at this point to me, it’s they saw a significant significantly higher incidence of. I’ve played loads of ITP reservations as well as patients with who are very, very heavily pretreated. Now when the when the post vaccine rescue therapy was administered, it was effective was administered about 30% of patients and they they reported no serious bleeding events.
NOTE Confidence: 0.720235435454545
00:38:47.330 --> 00:38:49.510 From a patient with.
NOTE Confidence: 0.75235606875
00:38:51.620 --> 00:38:54.404 Patients with stable or
NOTE Confidence: 0.75235606875
00:38:54.404 --> 00:38:57.188 increased platelet count after.
NOTE Confidence: 0.75235606875
00:38:57.190 --> 00:38:58.354 The first vaccine,
NOTE Confidence: 0.75235606875
00:38:58.354 --> 00:39:00.692 so that was those 43 patients,
NOTE Confidence: 0.75235606875
00:39:00.690 --> 00:39:05.186 and after those number 26 patients have
NOTE Confidence: 0.75235606875
00:39:05.186 --> 00:39:08.610 platelet count, decreased below 30.
NOTE Confidence: 0.75235606875
00:39:08.610 --> 00:39:10.890 So factors that are found not
NOTE Confidence: 0.75235606875
00:39:10.890 --> 00:39:14.905 predictive of estimation were age,
NOTE Confidence: 0.75235606875
00:39:14.910 --> 00:39:18.250 presence of autoimmune disease.
NOTE Confidence: 0.75235606875
00:39:18.250 --> 00:39:20.620 They actually had access to two
NOTE Confidence: 0.75235606875
00:39:20.620 --> 00:39:22.949 surveys and they sort of tried.
NOTE Confidence: 0.75235606875
00:39:22.950 --> 00:39:26.160 They tried to validate their findings
NOTE Confidence: 0.75235606875
00:39:26.160 --> 00:39:30.584 and they they looked into these surveys.
NOTE Confidence: 0.75235606875
These are two surveys. One is from a base in the United States, one is from UK especially. They track the track. Similar data. And so they found that in indeed in patients who had platelet count decreased. There were a lot more people with splenectomy. And then when they looked into your CTP cohort. Also survey based they found sort of breakdown of similar. Similar breakdown of decreased platelets about the third of patients indeed had ITP assassinations,
and they also in the same survey found this book to me. Was the shade with a 2 fold increase of risk of decreasing in platelets by more than 50%. So they acknowledged the speed limitaciones that there’s no lack of. There’s there’s no unvaccinated control group 2. To compare, there was a possible selection bias because they were following a lot closer to the people who are had refractory GP already. They were they didn’t account
00:40:41.710 --> 00:40:43.220 for titration for concurrent sort
NOTE Confidence: 0.76842572
00:40:43.270 --> 00:40:44.908 of interventions in terms of how
NOTE Confidence: 0.76842572
00:40:44.908 --> 00:40:46.340 they affect the platelet count,
NOTE Confidence: 0.76842572
00:40:46.340 --> 00:40:48.194 including the titrations of the of
NOTE Confidence: 0.76842572
00:40:48.194 --> 00:40:49.831 the medications of the treatment
NOTE Confidence: 0.76842572
00:40:49.831 --> 00:40:51.877 that the patients were already on,
NOTE Confidence: 0.76842572
00:40:51.880 --> 00:40:54.112 and the technology that the possible
NOTE Confidence: 0.76842572
00:40:54.112 --> 00:40:56.030 overlap between cohort might effect
NOTE Confidence: 0.76842572
00:40:56.030 --> 00:40:57.890 might affect the platelet count,
NOTE Confidence: 0.76842572
00:40:57.890 --> 00:41:00.248 but overall they felt that the
NOTE Confidence: 0.76842572
00:41:00.248 --> 00:41:02.799 major point was that there was
NOTE Confidence: 0.76842572
00:41:02.799 --> 00:41:05.273 no bleeding in refractory TCP
NOTE Confidence: 0.76842572
00:41:05.273 --> 00:41:07.292 in refractory thrombocytopenia.
NOTE Confidence: 0.76842572
00:41:07.292 --> 00:41:09.870 Following vaccination and the major.
NOTE Confidence: 0.7417165027
00:41:12.180 --> 00:41:13.686 .0 there was like if it’s
NOTE Confidence: 0.7417165027
00:41:13.686 --> 00:41:14.690 if it’s a splenectomy.
Patients follow closer.

If it’s a patient, were the difficult control

ITP or heavily pretreated.

Follow them closer.

And so that was main main idea and then in a sort of in the in the post in a additional question sort of session

And so that was main main idea and then in a sort of in the in the post in a additional question sort of session

And so that was main main idea and then in a sort of in the in the post in a additional question sort of session

Actually would you, you know, give the second vaccine, and so the
presenter actually said that she usually.

She would actually recommend but with close observation.

Alright, so moving on to the second one so the second study was similar.

In fact, they just followed one another. This one is from.

Dutch study the benefit of this study was a prospective cohort, but the question was fairly similar to what happens in patients with ITP with pre-existing ITP when they receive COVID-19 vaccine. This study had a control arm.

It had about a similar twice as much patients,
00:42:26.316 --> 00:42:29.179 218 in about the same number of 200.

00:42:29.180 --> 00:42:30.086 Healthy controls.

00:42:30.086 --> 00:42:33.257 Breakdown of vaccine was a little different,

00:42:33.260 --> 00:42:35.759 most of them received Moderna that was.

00:42:35.760 --> 00:42:37.413 Holland come in.

00:42:37.413 --> 00:42:39.617 All healthy controls received.

00:42:39.620 --> 00:42:42.380 Moderna 15 patients required

00:42:42.380 --> 00:42:43.760 rescue treatment.

00:42:43.760 --> 00:42:47.913 Now this is a breakdown of the treatment

00:42:47.913 --> 00:42:52.554 that patients were received or were on.

00:42:52.560 --> 00:42:55.395 So quite a number were on steroids

00:42:55.395 --> 00:42:58.542 in at a time and then also

00:42:58.542 --> 00:43:02.034 about 10% were Hispanic to me,

00:43:02.040 --> 00:43:04.284 definition of ITP dissertation

00:43:04.284 --> 00:43:06.528 was fairly the same.
In fact, exactly the same.

And sorry and So what they?

What they found here on the graph below is that the.

Both pleasant count in both.

Patient stated patients actually decreased and they I believe decreased by 6.3% in both groups, so they didn’t really feel there.

In fact, this is the better image of that.

And so they further look
00:43:55.230 --> 00:43:56.960 into risk factors as well.

00:43:56.960 --> 00:43:59.564 And here they found interesting piece

00:43:59.564 --> 00:44:02.610 which is a contradicts the previous study.

00:44:02.610 --> 00:44:05.130 They found that split me actually was

00:44:05.130 --> 00:44:07.230 associated with increase of platelets,

00:44:07.230 --> 00:44:10.240 quite substantial cruise of platelets.

00:44:10.240 --> 00:44:14.585 And a current treatment was associated

00:44:14.585 --> 00:44:17.915 with a decrease of platelets and.

00:44:17.920 --> 00:44:21.376 Age was associated with small decrease

00:44:21.380 --> 00:44:23.148 in platelets following vaccinations.

00:44:25.350 --> 00:44:28.365 So this is again sort of a tally that

00:44:28.370 --> 00:44:31.138 3030 patients developing masturbations

00:44:31.138 --> 00:44:33.906 15 required rescue treatment.

00:44:33.910 --> 00:44:36.190 The bleeding they did report bleeding,

00:44:36.190 --> 00:44:39.502 and interestingly enough and and in

00:44:42.820 -- 00:44:44.886
00:44:39.502 --> 00:44:43.112 a post in a in a in a in a question
NOTE Confidence: 0.723092663333333
00:44:43.112 --> 00:44:45.629 period they were asked about this,
NOTE Confidence: 0.723092663333333
00:44:45.630 --> 00:44:48.174 so all the five bleeding episodes
NOTE Confidence: 0.723092663333333
00:44:48.174 --> 00:44:50.362 happened in patients with platelet
NOTE Confidence: 0.723092663333333
00:44:50.362 --> 00:44:52.499 count of higher than 100,000.
NOTE Confidence: 0.723092663333333
00:44:52.499 --> 00:44:58.020 And in fact one patient who had a
NOTE Confidence: 0.723092663333333
00:44:58.020 --> 00:45:00.150 fatal gastrointestinal bleeding
NOTE Confidence: 0.723092663333333
00:45:00.150 --> 00:45:04.820 it was not related to vaccination at all,
NOTE Confidence: 0.723092663333333
00:45:04.820 --> 00:45:14.916 it was comorbidities,
NOTE Confidence: 0.723092663333333
00:45:08.881 --> 00:45:10.260 and in fact in the patients who
NOTE Confidence: 0.723092663333333
00:45:10.260 --> 00:45:14.916 had a GI bleed fatal jab bleed,
NOTE Confidence: 0.723092663333333
00:45:14.920 --> 00:45:17.256 Few patients require transfusions
NOTE Confidence: 0.723092663333333
00:45:17.256 --> 00:45:19.008 over plated or.
It helps so the conclusions here is, it's actually kind of similar. The effect of code in vaccination is similar in health in healthy controls and ITP patients. Dissertations were only a few ITP patients. There was a good response to rescue treatment. And essentially vaccination is safe and monitoring is advised and is actually was recommended by ASH guidelines. Come and this is sort of the additional questions that they were asked. Somebody asked whether they check
for platelet antibodies and they said they did not evaluate for platelet antibodies directly, but there’s no association with high levels in healthy controls. So, I want to just finish up with this third study, which is ITP related studying. In fact, this is an interesting trial about use of BTK inhibitor will support NIP in refractory relapsed ITP’s. The premise of the of the trial was I think it was five for face,
one face, two sort of update on on the phase one phase two trial. The premise was that inhibitors modulate quite a bit of a number of different effector cells. B cells and macrophages. Then also signaling of the basilar receptor and inhibitors decrease our reactive antibodies in so there's a. There's an interest in evaluating this group of class of medications. Class of drugs in it P. And specifically. While I'm really Brittany was chosen because.
Is believed to be very selective, so out of different kinases it’s pretty selective. It inhibits quite nicely, but not others, rather occupy. It’s quite reversible. Well, so there’s association of play legation with liberty, but not as shown here when. Was tested against collagen. Specially associated with aggregation more than rules.
So the trial instant criteria was fairly straightforward, its response. It’s essentially adults response. They have to have at least had to have at least response to one prior treatment, and there’s no other available to them or not approved. And there should be at least two platelet count less than 30 thirty thousand brother on 2 occasions and concurrent therapists were allowed, including. There was a dose escalation as a phase one, but in kind of a phase two phase of it part of it they use.
00:48:38.208 --> 00:48:39.684 actually 400 milligrams VID,
NOTE Confidence: 0.592017207142857
00:48:39.690 --> 00:48:42.010 which I’ll show soon.
NOTE Confidence: 0.592017207142857
00:48:42.010 --> 00:48:44.910 Primary in point was essentially.
NOTE Confidence: 0.592017207142857
00:48:44.910 --> 00:48:47.480 Account of greater than 50,000
NOTE Confidence: 0.592017207142857
00:48:47.480 --> 00:48:50.050 on two occasion at least,
NOTE Confidence: 0.592017207142857
00:48:50.050 --> 00:48:53.842 and an increase of 2020 thousand of the
NOTE Confidence: 0.592017207142857
00:48:53.842 --> 00:48:56.990 baseline without use of rescue medication.
NOTE Confidence: 0.592017207142857
00:48:56.990 --> 00:48:59.503 And they actually had a long term
NOTE Confidence: 0.592017207142857
00:48:59.503 --> 00:49:01.970 extension also for 400 milligrams PID.
NOTE Confidence: 0.592017207142857
00:49:01.970 --> 00:49:04.000 And so here’s what happened.
NOTE Confidence: 0.592017207142857
00:49:04.000 --> 00:49:07.426 So this is kind of a overall study diagram,
NOTE Confidence: 0.592017207142857
00:49:07.426 --> 00:49:11.249 so this is the 400 the ID group.
NOTE Confidence: 0.592017207142857
00:49:11.249 --> 00:49:12.964 So this is 45 patients.
NOTE Confidence: 0.592017207142857
00:49:12.970 --> 00:49:16.954 And so here’s the results.
NOTE Confidence: 0.592017207142857
00:49:16.954 --> 00:49:20.750 So out of this 4518 that is 40% reached
NOTE Confidence: 0.592017207142857
00:49:20.750 --> 00:49:22.630 the primary endpoint so greater
00:49:22.706 --> 00:49:24.855 than 50 in with 20 greater than.

00:49:27.840 --> 00:49:31.248 50% fifty thousand increase.

00:49:31.250 --> 00:49:34.502 Sorry, greater than 50,000 platelet count

00:49:34.502 --> 00:49:36.586 increased 20,000 from the baseline,

00:49:36.586 --> 00:49:39.234 so that's 18 patients reached that end

00:49:39.234 --> 00:49:42.410 point and it was very rapid improvement,

00:49:42.410 --> 00:49:44.546 so this is it's probably hard to see.

00:49:44.550 --> 00:49:47.700 But this is days and so within,

00:49:47.700 --> 00:49:49.206 you know this is actually 20.

00:49:49.210 --> 00:49:52.208 I think it's 25 or 29 days,

00:49:52.208 --> 00:49:53.936 so it's a really rapid improvement

00:49:53.936 --> 00:49:55.350 and it's actually sustained.

00:49:55.350 --> 00:49:58.190 And of course these are not responders and

00:49:58.190 --> 00:50:01.260 you can see here that this is sort of a.

00:50:01.260 --> 00:50:03.290 Better.

NOTE Confidence: 0.80177619
Way to assess sort of duration of response.
So this is greater than 30 number
of number of weeks achieved.
And so they made a point
that it’s indeed very rapid,
very rapid increase in fact,
median time to greater than 30,000 level was achieved in 8.5 days.
greater than 30,000 + 20,000 above
the baseline in basically 12
the primary response was about a month,
so it’s very very rapid. And then they also showed the.
What happened in this long long extension?
Arms, so to speak, and they said that it’s basically it was quite robust.
Especially it’s a. It’s a maintain the maintained the
response alright and then adverse effects. Basically it’s all grade one grade,
one grade, two diarrhea and nausea, one grade, two diarrhea and nausea,
fatigue. And again this is all
about 400 milligrams twice a day,
so conclusions. Mr. Bracnet provides.
Inhibition of phagocytosis.

And 40% of patients on 40 milligram VID achieved endpoint primary endpoint at 18 patients. Response was rapid and was well tolerated and response was maintained.

So there's open going face the Luna three trial, which further will address this. This this modality in additional questions. I think there was nothing really particularly interesting, but they said there's no, nobody, nobody was on any. Antibiotic prophylaxis and there was no infections.
So I think in interest of time I finish, I stop here. If we have some questions, well, thank you all very much for those very informative and very clear presentations. If people do have questions, if they could put them in the chat that there are a couple there. Maybe we can start with those. You mentioned in your abstract with factor 11 deficiency that some patients bled despite getting fresh frozen plasma. What might be some alternatives to treat those individuals?
Or do you have any thoughts about why those people still had bleeding?

Yeah, it’s interesting. I mean the half life of factor X is long. I think about two days or so, which is intriguing, but I think something we’ve all experienced in practice.

I think that may happen, perhaps just the quantity effect or Lebanon is not concentrated. You know, you never maybe know exactly what you’re getting in the FP, and maybe one element.

And I, you know there are cases reported of inhibitors,
so perhaps some of those patients that didn’t respond, maybe inhibitors. I think that I think Novoseven could be used, but I think with caution and maybe particularly in someone who had an inhibitor. I think there would be a role there, and then maybe sort of leaning more heavily on anti fibrinolytics might be useful, but I mean I think it’s. A challenge we’ve all seen and experienced that sometimes is hard to pinpoint.
Thank you and and Sudan shoe. You.
You mentioned that there was an increase in the clinical clinically relevant non major bleeding and individuals who are getting doax for cancer associated thrombosis. So when you prescribe either a low molecular weight heparin orado act to a patient with cancer associated thrombosis, how do you? Are there things about the patient that may point you. Decide on the benefits, risks there, and what agents do. You tend to choose and are there. Are there things about the patient that may point you.
One Direction or another?

So the clinically relevant non major bleeding was really of concern,
which was higher in doax and that has been pretty consistent throughout all the six trials.
So it wasn’t just one study.
And the way it impacts my practice is if I do look at the patient’s underlying bleeding risk.
If there isn’t an individual where I would be more concerned about bleeding,
perhaps someone who had immediate postoperative thrombotic event, or perhaps with somebody who’s going
for a surgery or has a known history of underlying bleeding or faults. I might be more inclined to use those individuals rather than doax, so that would be my approach and. How I would use that information? Thank you very much, don’t you? And Alex, are there any situations in which you might hold off on giving COVID vaccine? So individuals who are recently flared or have very low platelet counts and requiring intense therapy, for instance? You know, so this is interesting.
because the data they really didn’t actually include specifically, like they didn’t address the question of whether patients who were right, or right now on inactive.

ITP destinations, prior to vaccination. They were. They only had patients who were on chronic therapy, so I don’t think we have data per say in that regard, but personally, I think if there’s a flare actually flare, I probably would hold off, just not to disturb. You know it. You know,
in response further, I think it would might what might be really interesting is in this situation to address further whether they’re truly. Antibody platelet antibody, which none of them really looked into. Great, but but I think I would probably hold off until there’s some stabilization of platelet count. Seems very prudent. Yep, OK, alright. Well it’s it’s just about 1:00 o’clock, so I want to thank our speakers for again. Excellent presentation that were informative and I think highlighted some really important areas in classical hematology.
And thank you all for joining us.

Thank you very much.

Have a great day everyone. I.