Welcome to the Yale Ash 2021 highlights. My name is Bob Bone, 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 medicine 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.
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. This was presented at the plenary scientific session by Doctor Gayoung from University of Southern California. This was presented at the plenary scientific session by Doctor Gayoung from University of Southern California. This was presented at the plenary scientific session by Doctor Gayoung from University of Southern California. 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.
00:03:17.400 --> 00:03:19.413 thereby partially silencing
NOTE Confidence: 0.734905561428571
00:03:19.413 --> 00:03:22.097 the expression of antithrombin.
NOTE Confidence: 0.734905561428571
00:03:22.100 --> 00:03:24.220 This rebalances hemostasis and
NOTE Confidence: 0.734905561428571
00:03:24.220 --> 00:03:26.340 restores thrombin generation in
NOTE Confidence: 0.734905561428571
00:03:26.340 --> 00:03:28.672 patients with hemophilia or A
NOTE Confidence: 0.734905561428571
00:03:28.672 --> 00:03:31.060 and has been demonstrated to be
NOTE Confidence: 0.734905561428571
00:03:31.060 --> 00:03:33.233 effective in patients with or
NOTE Confidence: 0.734905561428571
00:03:33.233 --> 00:03:35.363 without inhibitors as I'll discuss.
NOTE Confidence: 0.734905561428571
00:03:35.370 --> 00:03:37.090 This study demonstrated that
NOTE Confidence: 0.734905561428571
00:03:37.090 --> 00:03:39.240 prophylactic use of the two
NOTE Confidence: 0.734905561428571
00:03:39.240 --> 00:03:41.032 strands significantly reduced
NOTE Confidence: 0.734905561428571
00:03:41.032 --> 00:03:42.967 annualized bleeding rates,
NOTE Confidence: 0.734905561428571
00:03:42.970 --> 00:03:44.446 which is essentially bleeding
NOTE Confidence: 0.734905561428571
00:03:44.446 --> 00:03:46.660 events on an annual basis in
NOTE Confidence: 0.734905561428571
00:03:46.731 --> 00:03:48.766 patients with hemophilia A or
NOTE Confidence: 0.734905561428571
00:03:48.766 --> 00:03:50.801 hemophilia B that have inhibitors,
and demonstrated both efficacy and safety data. In this study, 57 patients were randomized to one in an open label phase. Three trial patients were males over the age of 12, again with either hemophilia A or B. Eight patients in the phase, two Syrian group and the dosing of this medicine 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, which by a validated quality of life tool and also 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 and this was demonstrated to be extremely effective.

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 for two strand and nine patients received it in the hemophilia A category and we received for two strand and nine patients received it in the hemophilia B category. And again this is compared with the second second line here. But patient to receive that bypassing 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 given monthly and subcutaneous, which is a tremendous change in 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
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.
00:08:43.470 --> 00:08:44.709 Some background information.
00:08:44.709 --> 00:08:46.361 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.
00:08:50.504 --> 00:08:53.940 This has been seen in up to 30% of these patients.
00:08:55.631 --> 00:09:00.365 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.
00:09:11.990 --> 00:09:14.838 So the question this study has is what
proportion of patients with either persistent or chronic phase ITP and no recent exposure to any potentially curative therapy such as splenectomy or rituximab, achieve a long term remission off treatment at 24 weeks and 52 weeks. After having on at least three months of their TPO receptor agonist exposure, who had a complete response and persistent phase, ITP is defined as those with ITP between 3 and 12 months, whereas chronic phases lasting for beyond 12 months, so the inclusion criteria. So again, this was a nationwide prospective 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
TPRA agent and the patient could not have been receiving any concomitant steroid or corticosteroid 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 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 investigator’s 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 look 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
achieved 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, 27 had a complete response, 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 weeks or 52 weeks with the median platelet count of 31,000 at that time. No severe bleeding episodes occurred. They could not identify any predictive factors. Neither age, which agent the patient had,
how long they’d had.

I don’t know any of these things were

able to predict which patients

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,

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 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
dose of TPRS and patients who do
NOTE Confidence: 0.871721324333333
NOTE Confidence: 0.871721324333333
00:14:13.230 --> 00:14:14.623 And there may be opportunity for us
NOTE Confidence: 0.871721324333333
00:14:14.623 --> 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, or 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
00:16:21.162 --> 00:16:23.052 factor 11 levels were independently
NOTE Confidence: 0.892415406666667
00:16:23.052 --> 00:16:25.200 associated with the bleeding endpoint.
NOTE Confidence: 0.88016542
00:16:28.000 --> 00:16:31.396 Interestingly, 8 out of 21 patients,
NOTE Confidence: 0.88016542
00:16:31.400 --> 00:16:34.238 38% who suffered a bleeding complication.
NOTE Confidence: 0.88016542
00:16:34.240 --> 00:16:38.280 This happened despite prophylactic FFP.
NOTE Confidence: 0.88016542
00:16:38.280 --> 00:16:40.434 The mean factor level level for
NOTE Confidence: 0.88016542
00:16:40.434 --> 00:16:42.367 with patients who receive neuraxial
NOTE Confidence: 0.88016542
00:16:42.367 --> 00:16:44.959 anesthesia was 50 units per deciliter.
NOTE Confidence: 0.88016542
00:16:44.960 --> 00:16:46.910 In five patients with a
NOTE Confidence: 0.88016542
00:16:46.910 --> 00:16:48.080 negative bleeding history,
NOTE Confidence: 0.88016542
00:16:48.080 --> 00:16:49.499 despite surgical challenges,
NOTE Confidence: 0.88016542
00:16:49.499 --> 00:16:51.864 we’re actually able to receive
NOTE Confidence: 0.88016542
00:16:51.864 --> 00:16:53.226 neuraxial anesthesia effector
NOTE Confidence: 0.88016542
00:16:53.226 --> 00:16:55.320 level levels less than 10 and
NOTE Confidence: 0.88016542
00:16:55.320 --> 00:16:57.260 without any bleeding complications,
NOTE Confidence: 0.88016542
00:16:57.260 --> 00:16:59.342 and only one of these had
received prophylactic FFP.

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.

It just took sort of one event in time to define a personal history of bleeding factor.

11 levels were found to correlate with a slightly lower but statistically significant odds of surgical bleeding, and they found that a factor.

11 level cutoff of 40 units per
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 like to present is 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 willibrand 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 ISTHNF&SH 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.
noticed or seeking cofactor activity
or any abnormal one will event factor
measurements and also selected for those
who had diagnosis of atrial fibrillation.
The primary endpoint was rate of major
bleeding as defined by the IST criteria,
which is fatal.
Bleeding, bleeding in critical
organs or bleeding causing more
than two grams of two grams per DL,
drop in hemoglobin or more than two
units of red blood cell transfusion.
Sorry with the typo.
The results were that patients in
tribulation patients were between
00:21:04.730 --> 00:21:08.780 diagnosed between 1980 and 2020.

NOTE Confidence: 0.855000820476191

00:21:08.780 --> 00:21:09.616 For 340,

NOTE Confidence: 0.855000820476191

00:21:09.616 --> 00:21:11.288 patients were screened and

NOTE Confidence: 0.855000820476191

00:21:11.288 --> 00:21:12.960 89 patients were selected.

NOTE Confidence: 0.855000820476191

00:21:12.960 --> 00:21:14.880 For the final analysis.

NOTE Confidence: 0.855000820476191

00:21:14.880 --> 00:21:18.490 Out of those 64 patients were female,

NOTE Confidence: 0.855000820476191

00:21:18.490 --> 00:21:19.915 28% patients were deceased at

NOTE Confidence: 0.855000820476191

00:21:19.915 --> 00:21:21.690 the time of the data pool.

NOTE Confidence: 0.855000820476191

00:21:21.690 --> 00:21:25.650 Medium Chance Best Score was three and 89,

NOTE Confidence: 0.855000820476191

00:21:25.650 --> 00:21:29.708 so close to 90% had a score of two or higher.

NOTE Confidence: 0.855000820476191

00:21:29.710 --> 00:21:31.894 A third of the patients also had

NOTE Confidence: 0.855000820476191

00:21:31.894 --> 00:21:34.130 a quote acute coronary syndrome,

NOTE Confidence: 0.855000820476191

00:21:34.130 --> 00:21:36.110 which the authors lumped together

NOTE Confidence: 0.855000820476191

00:21:36.110 --> 00:21:38.090 STEMI non STEMI and Angela.

NOTE Confidence: 0.853843228181818

00:21:40.990 --> 00:21:45.310 In the in the figure over here as we can see,

NOTE Confidence: 0.853843228181818

00:21:45.310 --> 00:21:47.890 42.7% of the patients in the
00:21:47.890 --> 00:21:50.362 study were on aspirin or they
00:21:50.362 --> 00:21:51.866 were ever prescribed aspirin.
00:21:51.870 --> 00:21:56.854 About 13.4% of the patients were ever
00:22:01.100 --> 00:22:04.700 prescribed P2Y2 inhibitors and 56.2%
00:22:04.700 --> 00:22:08.418 The green color represents people
00:22:08.418 --> 00:22:11.694 with antiplatelet agents who also had
00:22:14.280 --> 00:22:18.890 About 1/4 of the patients were
00:22:17.046 --> 00:22:18.890 never prescribed any anticoagulant
00:22:18.968 --> 00:22:20.528 or antiplatelet agent.
00:22:23.270 --> 00:22:25.974 In these two graphs we can see the
00:22:25.974 --> 00:22:28.320 median time to 1st bleeding event
00:22:28.320 --> 00:22:30.702 on the left we have antiplatelet
00:22:30.783 --> 00:22:33.495 agents and on the right it’s
anticoagulants as we can see in both. It looked like the 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.
so these were the patients who never got antiplatelet therapy or anticoagulant therapy.

Concomitant anticoagulant and antiplatelet agents resulted in much higher risk of bleeding, which was about 28 events per hundred patient years.

The lifetime risk of major beating was also calculated by the investigators, which was 32% in those who were ever prescribed anticoagulants, and 25.6% who were never prescribed anticoagulants, and there was no statistical
00:23:46.845 --> 00:23:48.880 difference between the two groups.
NOTE Confidence: 0.879458732
00:23:51.020 --> 00:23:52.460 Looking at the stroke risk,
NOTE Confidence: 0.879458732
00:23:52.460 --> 00:23:54.960 the incidence of stroke was
NOTE Confidence: 0.879458732
00:23:54.960 --> 00:23:57.650 about 15 point 7%. And notably,
NOTE Confidence: 0.879458732
00:23:57.650 --> 00:24:00.065 11 out of the 14 patients had
NOTE Confidence: 0.879458732
00:24:00.065 --> 00:24:02.360 never used and equivalent for more
NOTE Confidence: 0.879458732
00:24:02.360 --> 00:24:04.771 than sorry had not been prescribed
NOTE Confidence: 0.879458732
00:24:04.771 --> 00:24:07.549 anticoagulant for 90 days or more.
NOTE Confidence: 0.879458732
00:24:07.550 --> 00:24:09.464 The median chance best score was
NOTE Confidence: 0.879458732
00:24:09.464 --> 00:24:11.500 three in those who had stroke.
NOTE Confidence: 0.709424477
00:24:13.740 --> 00:24:17.100 And and also those who are
NOTE Confidence: 0.709424477
00:24:17.100 --> 00:24:19.340 not anti quietly therapy.
NOTE Confidence: 0.709424477
00:24:19.340 --> 00:24:21.266 One of those patients who had
NOTE Confidence: 0.709424477
00:24:21.266 --> 00:24:25.510 a stroke had a fatal stroke.
NOTE Confidence: 0.709424477
00:24:25.510 --> 00:24:28.075 So the authors concluded that 50% of
NOTE Confidence: 0.709424477
00:24:28.075 --> 00:24:31.105 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.
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.

This was an update to the previous meta analysis,
which had four of these trials

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 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 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. 49.3% were Hispanics, 27.6% were non Hispanic blacks, 50.5% were non Hispanic whites and 7.6% were passed. Interestingly, 74.7% were uninsured. 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
patients with pancreatic or upper GI
cancers were the ones with highest
risk of cancer associated thrombosis.
The interesting part was the top.
Sorry, the bottom right figure where
we can see that non Hispanic black
population and non Hispanic white
population seem to have similar
cumulative incidence of cancer
associated thrombosis at 12 months.
While Hispanic population and Asian
population seem to have a lower risk,
so this contradicts what we have
traditionally known about thrombosis,
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 cancer 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.

I'm just gonna start my groups. The right one. Hopefully this is the right one.
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 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.

Several questions is in fact what is the effect of vaccines on platelet count, risk of bleeding events? 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 10 university affiliated patients that we actually also participated. So it’s 117 patients. With a pretty long history of ITP 12 years. And of course they were. You know at the time where the study was sort of conducted,
00:36:02.950 --> 00:36:03.618 yeah,
00:36:03.618 --> 00:36:06.958 the patients were getting vaccinated
00:36:06.958 --> 00:36:08.962 were older patients.
00:36:08.970 --> 00:36:12.760 So breakdown of what therapies
00:36:12.760 --> 00:36:14.276 were administered,
00:36:14.280 --> 00:36:16.752 either on therapy or off therapy
00:36:16.752 --> 00:36:18.400 or prior therapy.
00:36:18.400 --> 00:36:18.890 So
00:36:20.940 --> 00:36:24.600 TPO, RA's and we talk smack word
00:36:24.600 --> 00:36:26.620 bulk of the of the treatments,
00:36:26.620 --> 00:36:28.864 and colectomy was also in 21% of
00:36:28.864 --> 00:36:31.896 patients and at the time of the study 40
00:36:31.896 --> 00:36:34.514 patients were off treatment and 16 of
00:36:34.514 --> 00:36:37.319 those were with normal platelet count.
00:36:37.320 --> 00:36:38.830 This is a breakdown of.
See the exchange that we received.

Simon, of course majority and then definitions how they sort of were assessing the response. So stable platelet count was plus minus 20% of the pre vaccine level, and ITP exasperation was defined as either. Much higher than 50% reduction of platelet count or 20% reduction if the native platelets below 30,000 or the use of rescue treatment. They found that there’s a three groups of patients. 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 it was effective was administered about 30% of patients and they they reported no serious bleeding events.
From a patient with.

Patients with stable or increased platelet count after.

The first vaccine, so that was those 43 patients,

and after those number 26 patients have platelet count, decreased below 30.

So factors that are found not predictive of estimation were age, gender, vaccine type and presence of autoimmune disease.

They actually had access to two surveys and they sort of tried.

They tried to validate their findings and they looked into these surveys.
00:39:30.590 --> 00:39:32.334 These are two surveys.

NOTE Confidence: 0.75235606875

00:39:32.334 --> 00:39:34.750 One is from a base in the United States,

NOTE Confidence: 0.75235606875

00:39:34.750 --> 00:39:36.310 one is from UK especially.

NOTE Confidence: 0.75235606875

00:39:36.310 --> 00:39:37.638 They track the track.

NOTE Confidence: 0.76842572

00:39:39.680 --> 00:39:43.678 Similar data. And so they found

NOTE Confidence: 0.76842572

00:39:43.678 --> 00:39:46.752 that in indeed in patients who

NOTE Confidence: 0.76842572

00:39:46.752 --> 00:39:50.280 had platelet count decreased.

NOTE Confidence: 0.76842572

00:39:50.280 --> 00:39:51.660 There were a lot more

NOTE Confidence: 0.76842572

00:39:51.660 --> 00:39:54.470 people with splenectomy.

NOTE Confidence: 0.76842572

00:39:54.470 --> 00:39:57.320 And then when they looked

NOTE Confidence: 0.76842572

00:39:57.320 --> 00:40:02.685 into your CTP cohort.

NOTE Confidence: 0.76842572

00:40:02.685 --> 00:40:05.770 Also survey based they found

NOTE Confidence: 0.76842572

00:40:05.770 --> 00:40:07.406 sort of breakdown of similar.

NOTE Confidence: 0.76842572

00:40:07.406 --> 00:40:09.860 Similar breakdown of decreased

NOTE Confidence: 0.76842572

00:40:09.860 --> 00:40:11.284 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
for titration for concurrent sort
NOTE Confidence: 0.76842572
of interventions in terms of how
NOTE Confidence: 0.76842572
they affect the platelet count,
NOTE Confidence: 0.76842572
including the titrations of the of
NOTE Confidence: 0.76842572
the medications of the treatment
NOTE Confidence: 0.76842572
that the patients were already on,
NOTE Confidence: 0.76842572
and the technology that the possible
NOTE Confidence: 0.76842572
overlap between cohort might effect
NOTE Confidence: 0.76842572
might affect the platelet count,
NOTE Confidence: 0.76842572
but overall they felt that the
NOTE Confidence: 0.76842572
major point was that there was
NOTE Confidence: 0.76842572
no bleeding in refractory TCP
NOTE Confidence: 0.76842572
in refractory thrombocytopenia.
NOTE Confidence: 0.76842572
Following vaccination and the major.
NOTE Confidence: 0.7417165027
there was like if it’s
NOTE Confidence: 0.7417165027
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

following the abstract presentation.

Somebody was asking, how would you counsel

consultations and who actually did not,

perhaps did not who I had

from Selena after the first.

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,
218 in about the same number of 200.
Healthy controls.
Breakdown of vaccine was a little different, most of them received Moderna that was.
Holland come in.
All healthy controls received.
Moderna 15 patients required rescue treatment.
So quite a number were on steroids
in at a time and then also
about 10% were Hispanic to me,
definition of ITP dissertation
was fairly the same.
In fact, exactly the same.

And sorry, and so what they found here on the graph below is that both pleasant count in both normal controls and in patients actually decreased and they I believe it's decreased by 6.3% in both groups, so they didn't really feel there was a difference in reduction, but they both platelets went down.

In fact, this is the better image of that.
into risk factors as well.

And here they found interesting piece which is a contradicts the previous study. They found that split me actually was associated with increase of platelets, quite substantial cruise of platelets. And a current treatment was associated with a decrease of platelets and. Age was associated with small decrease in platelets following vaccinations. So this is again sort of a tally that 3030 patients developing masturbations 3030 patients developing masturbations 3030 patients developing masturbations 3030 patients developing masturbations 3030 patients developing masturbations. The bleeding they did report bleeding, and interestingly enough and and in
a post in a in a in a in a question
period they were asked about this,
so all the five bleeding episodes
happened in patients with platelet
count of higher than 100,000.
And in fact one patient who had a
fatal gastrointestinal bleeding
in the patients who had a GI bleed fatal jab bleed,
it was a severe liver disease.
Few patients require transfusions
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 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. So much much. He come. Well, so there's association of play legation with liberty, but not as shown here when. Was tested against collagen. So much much. He come. 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. 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 --> 00:49:11.249 And so here's what happened.
NOTE Confidence: 0.592017207142857
00:49:11.249 --> 00:49:12.970 So this is kind of a overall study diagram,
NOTE Confidence: 0.592017207142857
00:49:12.970 --> 00:49:14.946 so this is the 400 the ID group.
NOTE Confidence: 0.592017207142857
00:49:14.946 --> 00:49:16.954 So this is 45 patients.
NOTE Confidence: 0.592017207142857
00:49:16.954 --> 00:49:18.024 And so here's the results.
NOTE Confidence: 0.592017207142857
00:49:18.024 --> 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
than 50 in with 20 greater than.

50% fifty thousand increase.

Sorry, greater than 50,000 platelet count increased 20,000 from the baseline,

so that’s 18 patients reached that end

point and it was very rapid improvement,

so this is it’s probably hard to see.

But this is days and so within,

you know this is actually 20.

I think it’s 25 or 29 days,

so it’s a really rapid improvement

and it’s actually sustained.

And of course these are not responders and

you can see here that this is sort of a.

Better.
Way to assess sort of duration of response.

So this is greater than 30 number

in 20 and then 15 and 14.

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 baseline in greater than 50,000 play

account in just about the same

12.5 days and median time for 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

Especially it’s a.

It’s a maintain the maintained the

response alright and then adverse effects.

Basically it’s all grade 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 400 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 was on any.

Antibiotic prophylaxis and there was no infections.
00:52:18.100 --> 00:52:20.278 So I think in interest of time I finish,
00:52:20.280 --> 00:52:23.418 I stop here.
00:52:23.420 --> 00:52:25.080 If we have some questions, well,
00:52:25.090 --> 00:52:27.466 thank you all very much for those very
00:52:27.466 --> 00:52:29.499 informative and very clear presentations.
00:52:31.650 --> 00:52:33.000 If people do have questions,
00:52:33.000 --> 00:52:35.440 if they could put them in the chat
00:52:35.440 --> 00:52:37.409 that there are a couple there.
00:52:37.410 --> 00:52:39.408 Maybe we can start with those.
00:52:39.410 --> 00:52:40.742 So I’m Kelsey.
00:52:40.742 --> 00:52:43.406 You mentioned in your abstract with
00:52:43.406 --> 00:52:46.429 factor 11 deficiency that some patients
00:52:46.430 --> 00:52:50.330 bled despite getting fresh frozen plasma.
00:52:50.330 --> 00:52:52.124 What what might be some alternatives
00:52:52.124 --> 00:52:53.320 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 11 is long, I think about two days or so, it’s 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 FSP, 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 at a lower dose or 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. It’s a great question, great, thank you.
Thank you and Sudan shoe. You.

You mentioned that there was an increase in the clinical clinically relevant non major bleeding and individuals who are getting dox 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 what agents do. You tend to choose and are there.

Are there things about the patient that may point you
00:54:24.432 --> 00:54:25.780 in One Direction or another?

00:54:27.840 --> 00:54:30.594 So the clinically relevant non major bleeding was really of concern,

00:54:33.130 --> 00:54:34.894 which was higher in doax and

00:54:36.740 --> 00:54:38.820 throughout all the six trials.

00:54:38.820 --> 00:54:42.078 So it wasn’t just one study.

00:54:42.080 --> 00:54:44.271 And the way it impacts my practice

00:54:44.271 --> 00:54:46.981 is if if I do look at the patient’s underlying bleeding risk.

00:54:46.981 --> 00:54:48.544 If there isn’t an individual where I

00:54:48.544 --> 00:54:51.386 would be more concerned about bleeding,

00:54:51.386 --> 00:54:53.300 perhaps someone who had immediate

00:54:53.300 --> 00:54:56.250 postoperative thrombotic event,

00:54:56.250 --> 00:54:59.872 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 patients with ITP, and 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 in right, right, or right now on inactive.

They only had patients who were on sort of 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.
00:56:25.060 --> 00:56:28.168 in response further, further, further,
NOTE Confidence: 0.610153234285714
00:56:28.168 --> 00:56:30.728 I think it would might what might be
NOTE Confidence: 0.610153234285714
00:56:30.728 --> 00:56:33.003 really interesting is in in this situation
NOTE Confidence: 0.610153234285714
00:56:33.003 --> 00:56:35.687 to address further whether they’re truly.
NOTE Confidence: 0.610153234285714
00:56:35.690 --> 00:56:38.770 Uh and antibody platelet antibody,
NOTE Confidence: 0.610153234285714
00:56:38.770 --> 00:56:40.954 which none of them really looked into.
NOTE Confidence: 0.759774240235294
00:56:43.110 --> 00:56:44.699 Great, but but I think I would
NOTE Confidence: 0.759774240235294
00:56:44.699 --> 00:56:46.460 probably hold off until there’s some
NOTE Confidence: 0.759774240235294
00:56:46.460 --> 00:56:47.836 stabilization of platelet count.
NOTE Confidence: 0.7916155125
00:56:49.110 --> 00:56:52.600 Seems very prudent. Yep, OK, alright.
NOTE Confidence: 0.7916155125
00:56:52.600 --> 00:56:54.770 Well it’s it’s just about 1:00 o’clock,
NOTE Confidence: 0.7916155125
00:56:54.770 --> 00:56:58.358 so I want to thank our speakers for again.
NOTE Confidence: 0.7916155125
00:56:58.358 --> 00:56:59.594 Excellent presentation that
NOTE Confidence: 0.7916155125
00:56:59.594 --> 00:57:01.713 were informative and I think
NOTE Confidence: 0.7916155125
00:57:01.713 --> 00:57:03.361 highlighted some really important
NOTE Confidence: 0.7916155125
00:57:03.361 --> 00:57:05.009 areas in classical hematology.
And thank you all for joining us.

Thank you very much.

Have a great day everyone.