Mesenteric Venous Thrombosis as a Predictor of Target Artery Thrombosis and Trans-Arterial Micro Perfusion Treatment Completion Among Patients with Locally Advanced Pancreatic Cancer

Dr. David Sperling[1], Dr. Justin Lee[2], Dr. Sandeep Laroia[3], Dr. Paula Novelli[4], George Andary[5], Dr. Ramtin Agah[5], Dr. Michel Accad[5]

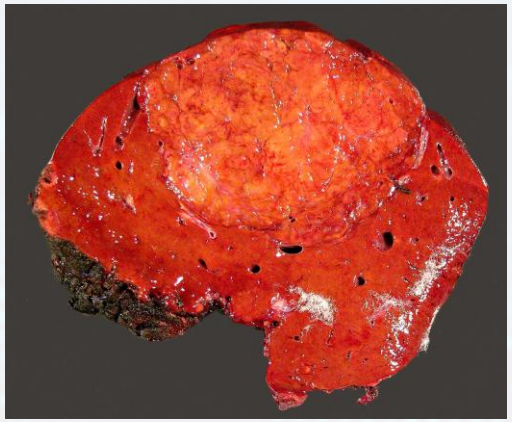
[1] Columbia University Irving Medical Center, New York, NY, United States; [2] Radiology Partners and Sarasota Memorial Hospital, Sarasota, FL, United States; [3] University of Iowa Hospitals & Clinics, Iowa City, IA, United States; [4] University of Pittsburgh Medical Center, Hillman Cancer Center, Pittsburgh, PA, United States; [5] RenovoRx, Inc., Los Altos, CA, United States

SIR 2024 MARCH 23–28 SALT LAKE CITY
SIRpass the summit

Society of Interventional Radiology

Chemotherapy is Not Effectively Delivered to Primary Pancreatic Tumors

Dense fibrotic stroma | Sparse tumor cellularity | Hypovascular tumors



Liver tumors are vascularized

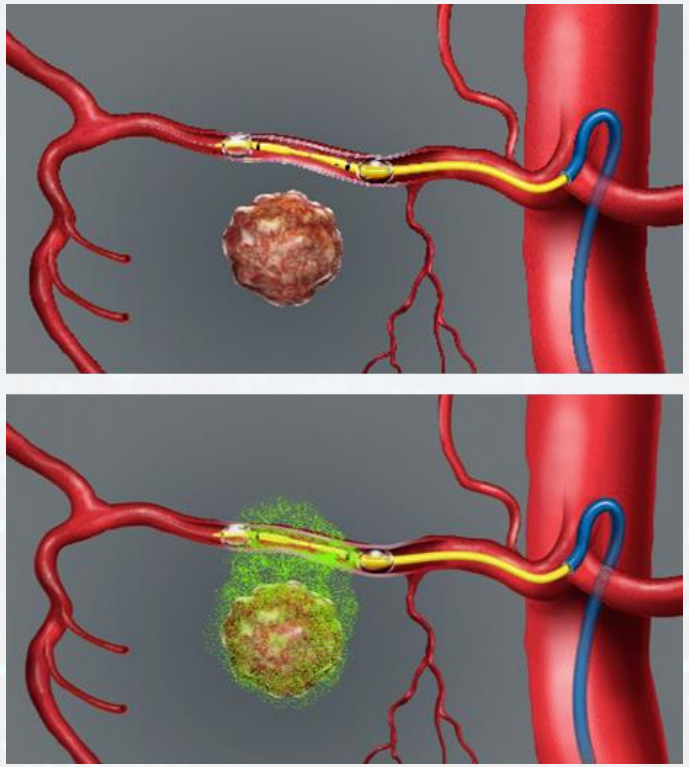
- Large tumor feeders – excellent targets for therapy
- Large branches within tumor - easily visualize tumor

Pancreas tumors are hypovascular

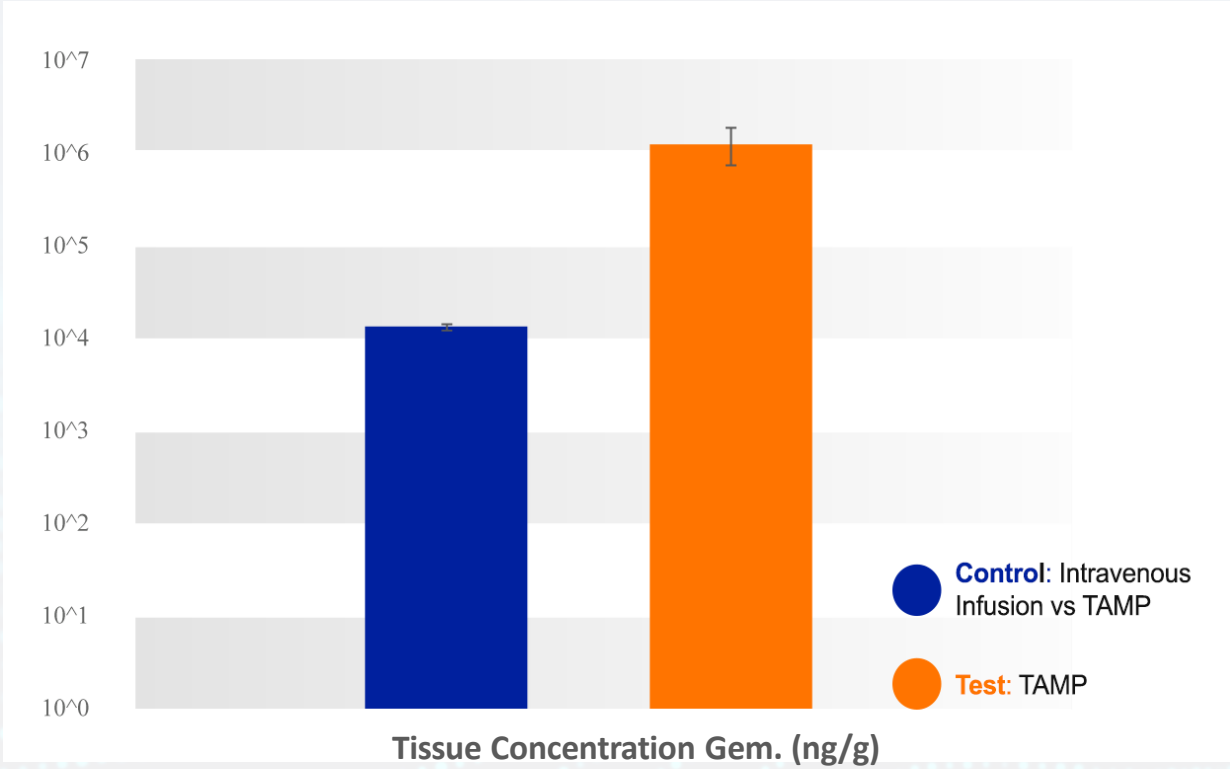
- Inability to identify tumor feeder vessels and penetrate drug into the tumor

Trans-Arterial Micro-Perfusion (TAMP): Method of Intra-arterial Delivery of Chemotherapy Independent of Feeder Vessels

Mechanism: after vessel isolation, increase in pressure forces drug across the artery wall into the micro-vasculature into tumor tissue

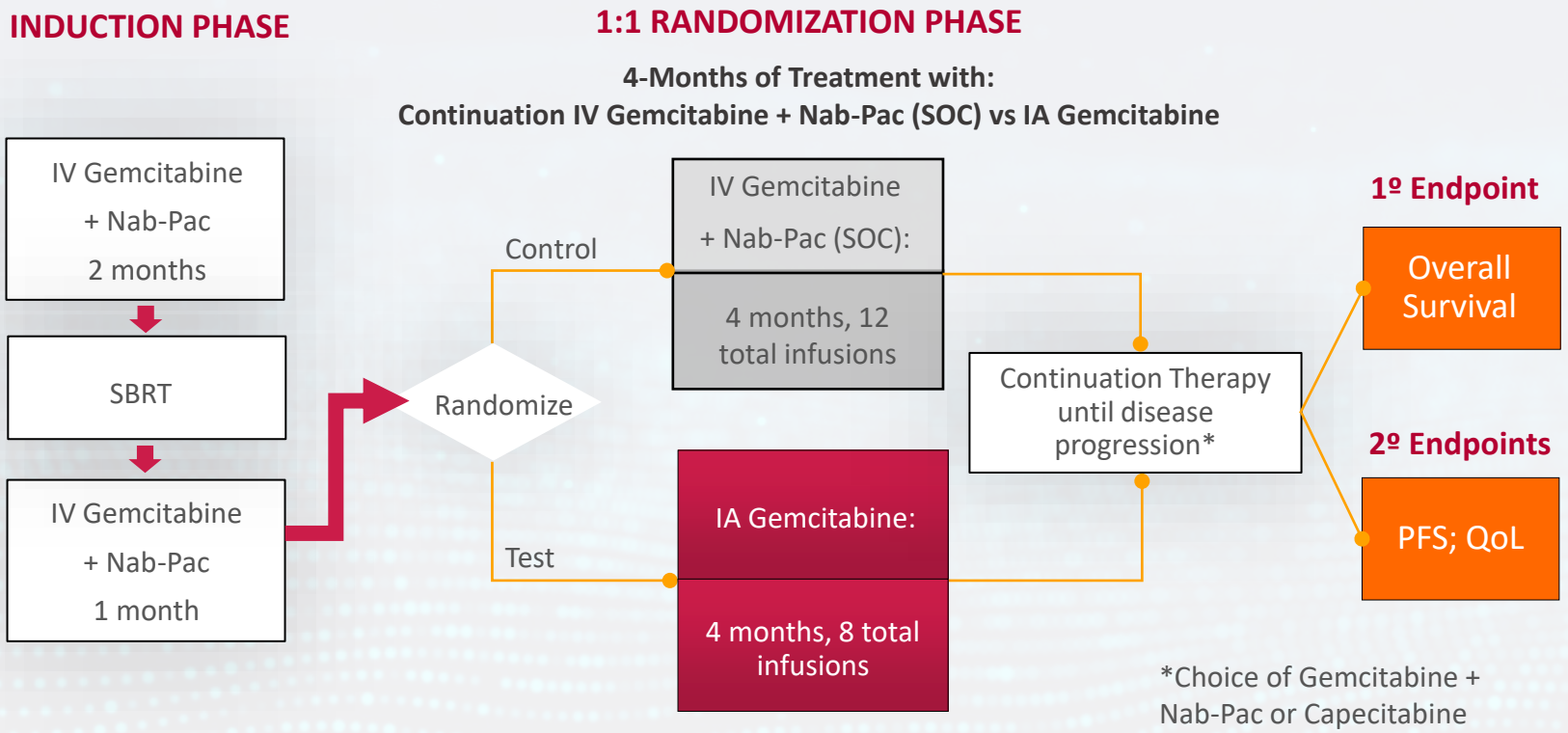


Increases Drug Concentration to Target Pathological Site by ~100X* Compared to IV Administration[1]



[1]K. Farsad, et al. Trans-pulmonary artery selective chemotherapy delivery to lung using a double balloon-occlusion catheter. *JVIR*. March 2019; 30 (3).

Phase III TIGeR-PaC Study: Trans(Intra)-arterial Gemcitabine vs. Continuation of IV Gemcitabine and Nab-Paclitaxel following Radiotherapy for Locally Advanced Pancreatic Cancer



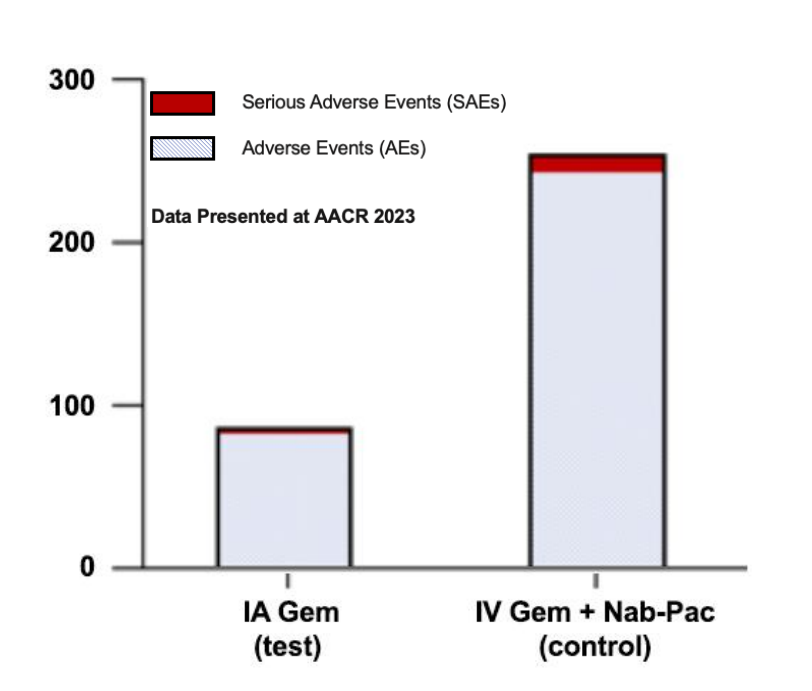
First Interim analysis: After 45 patient Randomized and 26 Events (published June 2023)

TIGeR-PaC: Tolerability and Safety of Treatment

Tolerability during active treatment:

- 61% of IA patients received all planned treatments at the pre-specified dose vs. 18% of IV (primarily due to AEs or SAEs)
- Patients receiving IA therapy had more nausea and abdominal pain events
- Patients receiving IV therapy had more myelosuppression, fatigue, dehydration, neuropathy, and metabolic derangements

65% fewer total AEs and SAEs in IA vs. IV arm

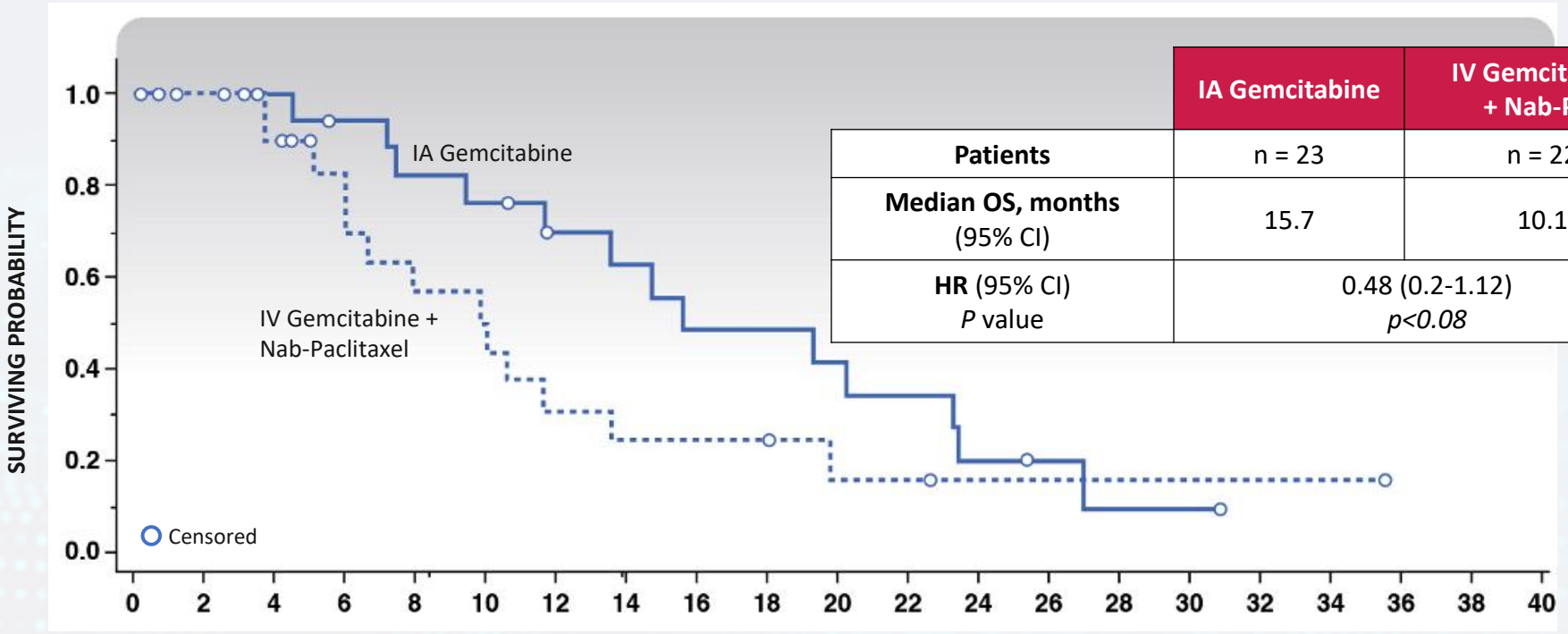


AEs with greater than 10% frequency in each arm (All Grades)

Adverse Events	IV Gem + Nab-Pac	IA Gemcitabine
Neutropenia	81%	21%
Anemia	48%	8%
Thrombocytopenia	38%	4%
Elevated AST	33%	4%
Elevated ALT	29%	13%
Fatigue	19%	8%
Neuropathy	19%	0%
Dehydration	19%	8%
Hypertension	14%	4%
Hypokalemia	14%	4%
Hypoalbunemia	14%	4%
Abdominal Pain	0%	21%
Nausea	0%	21%

Adverse event prevalence: IA IV

TIGeR-PaC Primary Endpoint: Overall Survival



	IA Gemcitabine	IV Gemcitabine + Nab-Pac
Patients	n = 23	n = 22
Median OS, months (95% CI)	15.7	10.1
HR (95% CI) *P* value	0.48 (0.2-1.12) *p<0.08*	

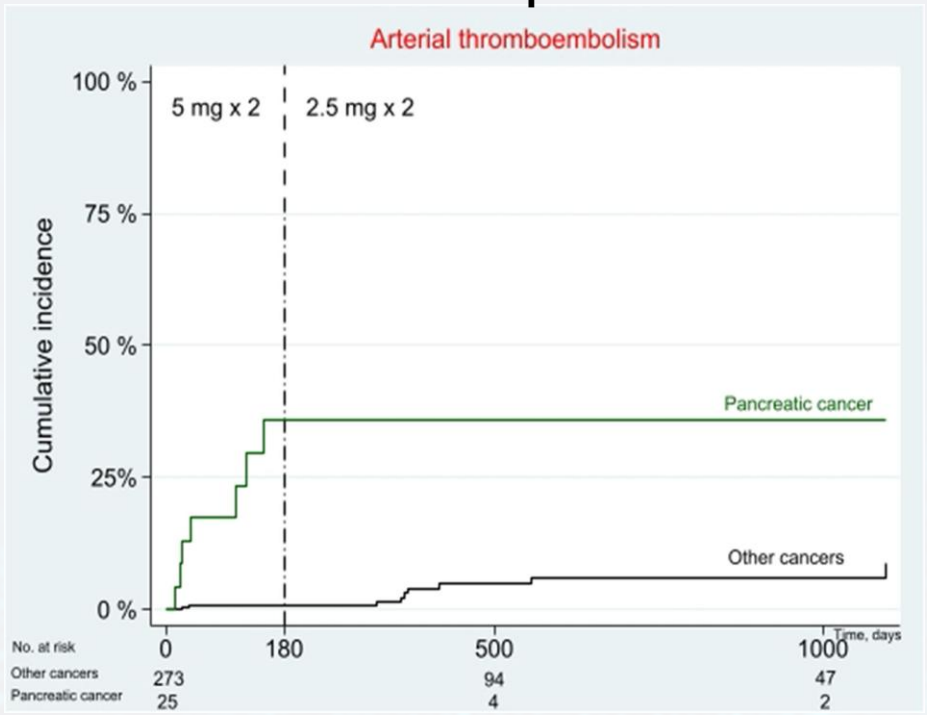
Limitation for Repeat Procedure: Arterial Thrombosis

- At first interim analysis, 61% of TIGeR-PaC IA patients received all planned treatments at the pre-specified dose
- Of the 39% that did not receive all planned procedures, the major reason was arterial thrombosis during attempt for repeat procedure

Thrombosis in Pancreatic Cancer

- Patients are at risk of both arterial (ATE) and venous thrombo-embolism (VTE), although the incidence of VTE is higher than ATE
- PDAC carries the highest risk of VTE among all cancers, with rates of 5%–41% in retrospective cohorts and up to 67% in postmortem[1]
- ATE is less well defined in PDAC: 5.9% in first 6 months after diagnosis[2]
- In PDAC patients with VTE, the risk of AE is reported to be as high as 37% despite use of DOAC[3]

Arterial Thromboembolism in Cancer Patients Treated with Apixaban



Trine-Lise Larsen, et al. Arterial Thromboembolism in Cancer Patients Treated with Apixaban. *Blood.* 2022; 140 (Suppl 1):11366-11367. Figure 1.

[1]Corinne Frere, et al. Incidence of Venous Thromboembolism in Patients with Newly Diagnosed Pancreatic Cancer and Factors Associated with Outcomes. *Gastroenterology*. 2020;158:1346-1358.
[2]Babak B. Navi, et al. Risk of Arterial Thromboembolism in Patients with Cancer. *J Am Coll Cardiol*. 2017;70(8):926-938.
[3]Trine-Lise Larsen, et al. Arterial Thromboembolism in Cancer Patients Treated with Apixaban. *Blood*. 2022;140 (Suppl 1):11366-11367.

Can Risk of Arterial Thrombosis in TAMP be Predicted?

Key Questions:

- Is arterial thrombosis in TAMP patients related to increased hypercoagulable state? Or does it occur independently of patient predisposition for thrombosis, indicating a direct relationship to the TAMP procedure?
- Mesenteric vein thrombosis (MVT) is the most common form of VTE in these patients (30% of total VTE[1]). Can MVT be used as a correlate for hypercoagulable state to predict risk of arterial thrombosis with TAMP?

[1]Corinne Frere, et al. Incidence of Venous Thromboembolism in Patients with Newly Diagnosed Pancreatic Cancer and Factors Associated with Outcomes. *Gastroenterology*. 2020;158:1346-1358.

Relationship of Baseline MVT to Arterial Thrombosis with TAMP: METHODS

- Utilizing the TIGeR-PaC analysis results, we compared the incidence of arterial thrombosis in consecutive TAMP-randomized study participants with vs. without baseline MVT
- The presence or absence of MVT on baseline CT was determined by a core imaging center radiologist
- The outcomes examined were:
  1) Inability to complete the planned 8-cycles of TAMP
  2) Target vessel thrombosis during or after TAMP
  3) Assessment of peri-procedural pain or discomfort
- Statistical analysis was performed using the Student's *t*-test.

Relationship of Baseline MVT to Arterial Thrombosis with TAMP: RESULTS

- Of the 25 subjects randomized to TAMP therapy, 11 failed to complete 8 cycles of treatment.
- Of these 11 patients, 6 failed completion due to thrombosis of the targeted arterial artery (24% of total cohort)
- Among those 6 subjects, the prevalence of MVT (partial or complete) on baseline abdominal CT imaging was 100% (6/6), as compared to 57% (8/14) among subjects who were able to complete the 8 cycles of therapy and did not develop arterial thrombosis during TAMP treatment ($P = 0.004$).
- In addition, the incidence of procedural nausea and vomiting (clinical signs of abdominal ischemia) was more common in patients with MVT (57%) than in those without MVT (18%) ($P = 0.003$).

Conclusions

- TAMP is a novel technique for localized chemotherapeutic delivery with promising early clinical data for both survival and decreased side effects compared to conventional chemotherapy in patients with PDAC (TIGeR-PaC interim analysis results)
- The major limitation of TAMP for repeated procedure is arterial thrombosis (24% of cohort treated so far)
- Mesenteric venous thrombosis is a sensitive predictor for patients at risk of arterial thrombosis, likely related to patients risk of hypercoagulable state affecting both venous and arterial thrombosis

Extra Slide