Highlights from EHA

Novità dall'EHA >> [Trombosi e cancro]

Relatore: **A. FALANGA**

27-28 ottobre 2008

Borgo S. Luigi – Monteriggioni (Siena)

TROMBOSI E CANCRO

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- SIMPOSIO EDUCAZIONALE:
  - LMWH and cancer progression (M. Prins)
  - Hemostasis and cancer (FR Rickles)
  - Prophylaxis and treatment of venous thromboembolism in cancer (G. Agnelli)
- 3 PRESENTAZIONI ORALI
- 11 POSTER
- 6 SOLO PUBBLICAZIONE

TROMBOSI E CANCRO

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Cancer and Venous Thromboembolism (VTE)

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- VTE is a frequent complication of cancer:
  - Estimated risk is 0.5%/year or 0.04%/month
  - 6.5-fold increased risk with chemotherapy
    - *Heit JA et al, Arch Intern Med,2000*
    - *Lee AYY, Br J Haematol, 2004*
- Cancer-associated VTE has several consequences:
  - Increased mortality
  - Increased risk of recurrent VTE as well as bleeding complications
  - Interruption of chemotherapy
  - Economic implications
    - *Levitan et al, 1999; Sorensen et al, 2000; Prandoni et al, 2002; Khorana A et al, 2006*

Incidence of VTE in US Cancer Patients: 1979-1999

(National Hospital Discharge Survey data. Stein PD et al. Am J Med. 2006)

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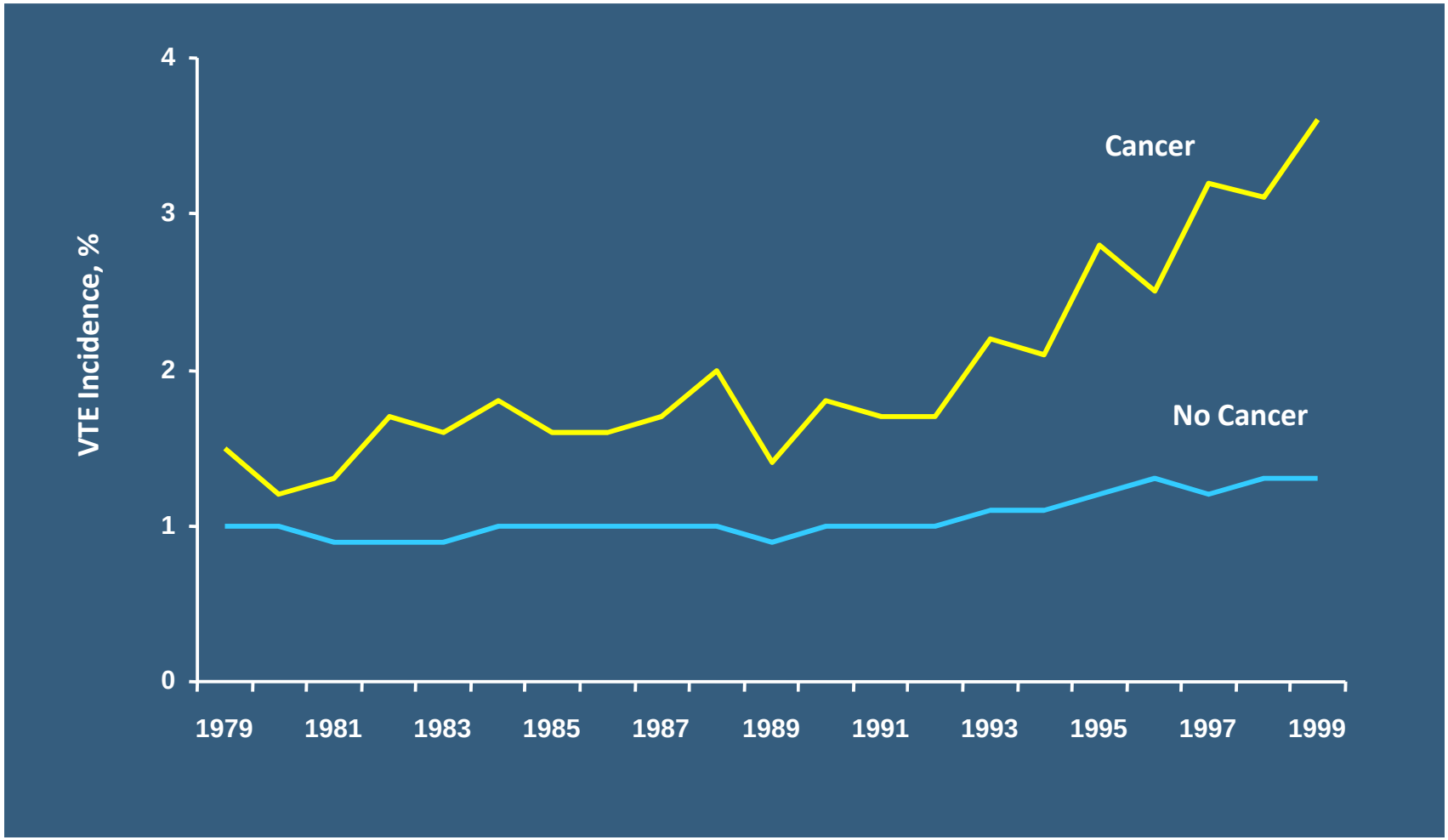

VTE Prevention: Prophylaxis under-utilized

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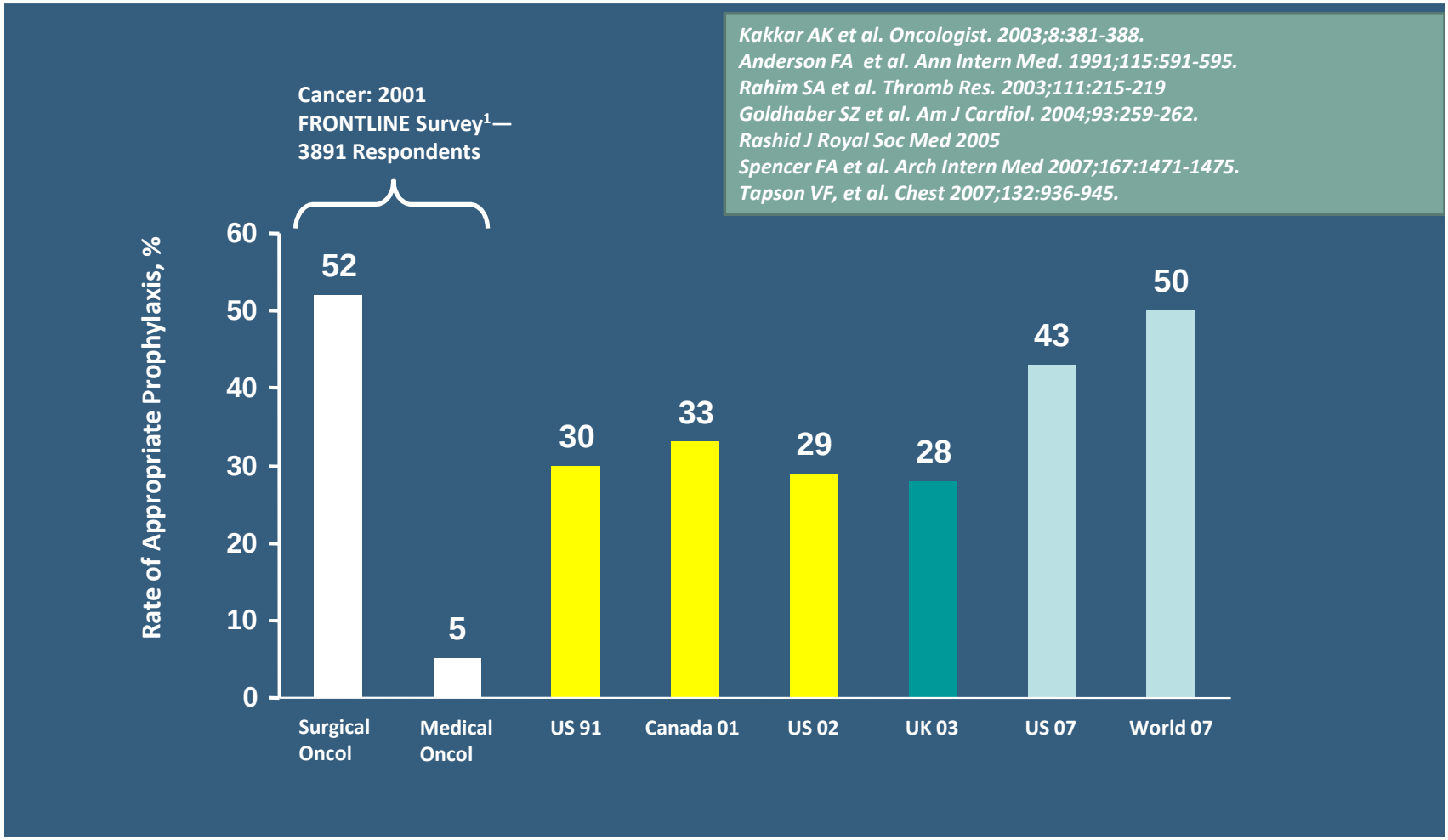

Major Risk Factors

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- Age
- Primary site of cancer (gastrointestinal, brain, lung, gynecologic, pancreatic, ovarian, renal, bladder, hematologic)
- History of VTE
- Hospitalization
- Major surgery
- Those receiving active therapy, including chemotherapy, antiangiogenic drugs, and hormonal therapy
- Metastatic disease
- Red cell growth factors

Risk Factors for Chemotherapy-associated VTE

(Khorana et al., Blood 2008)

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Patient Characteristic	Risk Score
Site of cancer: stomach, pancreas	2
Site of cancer: lung, lymphoma, gynaecologic, bladder, testicular	1
Platelet count > 350,000/mm3	1
Haemoglobin < 10 g/dl or use of erythropoietin	1
Leukocyte count > 11,000/ mm3	1
Body mass index > 35	1

Low risk:	score 0
Intermediate risk:	score 1-2
High risk:	score $\leq$ 3

Guidelines for VTE Prophylaxis and Treatment in Patients with Cancer Released by National and International Scientific Societies

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- AIOM (Società Italiana Oncologia Medica)
- ASCO (American Society of Clinical Oncology)
- NCCN (National Comprehensive Cancer Network)
- ESMO (European Society of Medical Oncology)

- ACCP (American College of Chest Physicians)
- IUA (International Union of Angiology)
- SISET (Società Italiana per lo Studio dell'Emostasi e della Trombosi)

Tromboembolismo venoso nel paziente oncologico EHA

Abstracts: *DIAGNOSI, PROFILASSI, TERAPIA*

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N°	TITOLO	Autore corrispondente
375°	SYMPTOMATIC VENOUS THROMBOEMBOLISM IN MEDICAL IN-PATIENTS: A MULTICENTER ITALIAN SURVEY ON PREVALENCE, RISK ASSESSMENT, AND ATTITUDE TOWARDS PROPHYLAXIS.	Gussoni et al. (Roma, ITALY)
878 °	BEST PRACTICES IN QUALITY AND SAFETY ON PATIENT CARE: ROSWELL PACK CANCER INSTITUTE QUALITY INITIATIVE IN VENOUS THROMBOEMBOLISM PROPHYLAXIS (VTE) FOR THE ONCOLOGY POPULATION	Padmanabhan et al. (NY, USA)
865°	LOW-MOLECULAR-WEIGHT HEPARIN (LMWH) TREATMENT IN ACUTE LEUKEMIA (AL) PATIENTS WITH SEVERE THROMBOCYTOPENIA AND CONCOMITANT VENOUS OR ARTERIAL THROMBOSIS	Cedrone et al. (Roma, ITALY)
151°	UNUSUAL VEIN THROMBOSIS IN PATIENTS WITH POLYCYTHEMIA VERA (PV) AND ESSENTIAL THROMBOCYTHEMIA (ET)	Randi et al. (Padova, ITALY)
1065	CEREBRAL VENOUS SINUS THROMBOSIS AS A COMPLICATION OF ASPARAGINASE TREATMENT IN A 15 YEAR-OLD GIRL WITH T CELL NON-HODGKIN LYMPHOMA	Ociepa et al. (Szczecin, POLAND)
1371	ABDOMINAL VEIN THROMBOSIS ASSOCIATED WITH LUPUS ANTICOAGULANT AS THE FIRST CLINICAL FEATURE OF MYELOPROLIFERATIVE DISEASE	Jamrozek-Jedlińska et al. (Poznań, POLAND)

Tromboembolismo venoso nel paziente oncologico EHA

Abstracts: *MIELOMA MULTIPLO*

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N°	TITOLO	Autore corrispondente
910*	ENOXAPARIN VERSUS ASPIRIN VERSUS LOW-FIXED-DOSE OF WARFARIN IN NEWLY DIAGNOSED MYELOMA PATIENTS TREATED WITH THALIDOMIDE-CONTAINING REGIMENS: A RANDOMIZED, CONTROLLED TRIAL	Palumbo et al. (Torino, ITALY)
913*	THROMBOPHILIC ALTERATIONS AND RISK OF VENOUS THROMBOEMBOLISM IN NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS TREATED WITH THALIDOMIDE AND HIGH-DOSE DEXAMETHASONE	Zamagni et al. (Bologna, ITALY)
638 °	EFFECT ON SURVIVAL OF LENALIDOMIDE AND DEXAMETHASONE ASSOCIATED DEEP VEIN THROMBOSIS (DVT) IN RELAPSED MULTIPLE MYELOMA PATIENTS	Zangari et al. (Salt Lake City, USA)

Tromboembolismo venoso nel paziente oncologico

EHA Abstracts: *FATTORI DI RISCHIO*

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N°	TITOLO	Autore corrispondente
358°	CLOTTING FACTOR VIII AND RISK OF VENOUS THROMBOEMBOLISM IN CANCER PATIENTS – RESULTS OF THE VIENNA CANCER AND THROMBOSIS STUDY	Vormittag et al. (Vienna, AUSTRIA)
750°	THE V617F JAK 2 MUTATION IS NOT A FREQUENT EVENT IN PATIENTS WITH CEREBRAL VENOUS THROMBOSIS WITHOUT OVERT CHRONIC MYELOPROLIFERATIVE DISORDER (MPD)	Bellucci et al. (Paris, FRANCE)
145°	ABSENCE OF THE JAK2 EXON 12 MUTATIONS IN PATIENTS WITH SPLANCHNIC VENOUS THROMBOSIS AND WITHOUT OVERT CHRONIC MYELOPROLIFERATIVE DISORDERS	Fiorini et al. (Roma, ITALY)
752°	CORRELATION BETWEEN LEUKOCYTOSIS AND THROMBOSIS IN PHILADELPHIA NEGATIVE CHRONIC MYELOPROLIFERATIVE DISEASES.	Caramazza et al. (Palermo, ITALY)
1032	INCIDENCE OF ALTERATIONS OF COAGULATION ON THE RISK OF THROMBOSIS IN ESSENTIAL THROMBOCYTEMIA	Padron Rodriguez et al. (Zaragoza, SPAIN)
1370	INCIDENCE OF JAK2 V617F TYROSINE KINASE MUTATION AND ITS CORRELATION WITH THROMBOSIS AND BLEEDING COMPLICATIONS IN PATIENTS WITH CHRONIC MYELOPROLIFERATIVE DISORDERS	Marton et al. (Szombathely, HUNGARY)
1216	A SHORT ACTIVATED PARTIAL THROMBOPLASTIN TIME HAS NO CORRELATION WITH THE VENOUS DRAW LINE THROMBOSIS IN PATIENTS WITH HAEMATOLOGICAL MALIGNANCIES UNDERGOING PERIPHERAL BLOOD STEM CELL HARVEST	Kumar et al. (Cambridgesshire, UK)
1064	THE ROLE OF PROTHROMBOTIC GENETIC RISK FACTORS ON DEVELOPMENT OF THROMBOSIS IN PEDIATRIC ONCOLOGY PATIENTS	Turker et al. (Izmir, TURKEY)

Trombosi idiopatica e cancro occulto

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N°	TITOLO	Autore corrispondente
361°	CANCER-RELATED VENOUS THROMBOSIS: RESIDUAL VEIN THROMBOSIS IMPROVES SCREENING FOR OCCULT CANCER	Siragusa et al. (Palermo, ITALY)

I meccanismi di Trombosi sono coinvolti nella crescita e disseminazione tumorale

Tromboembolismo venoso nel paziente oncologico:
Abstracts: PATOGENESI

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N°	TITOLO	Autore corrispondente
366°	ENDOTHELIUM PROCOAGULANT AND ANGIOGENIC ACTIVITIES INDUCED BY ACUTE PROMYELOCYTIC LEUKEMIA (APL) CELLS ARE INHIBITED BY LOW MOLECULAR WEIGHT HEPARINS (LMWH)	Vignoli et al. (Bergamo, ITALY)
912*	ARSENIC TRIOXIDE (AS2O3) MODULATES THE PROCOAGULANT ACTIVITIES OF FRESHLY ISOLATED ACUTE PROMYELOCYTIC LEUKEMIA (APL) BLASTS: A COMPARISON WITH ALL-TRANS RETINOIC ACID (ATRA)	Balducci et al. (Bergamo, ITALY)

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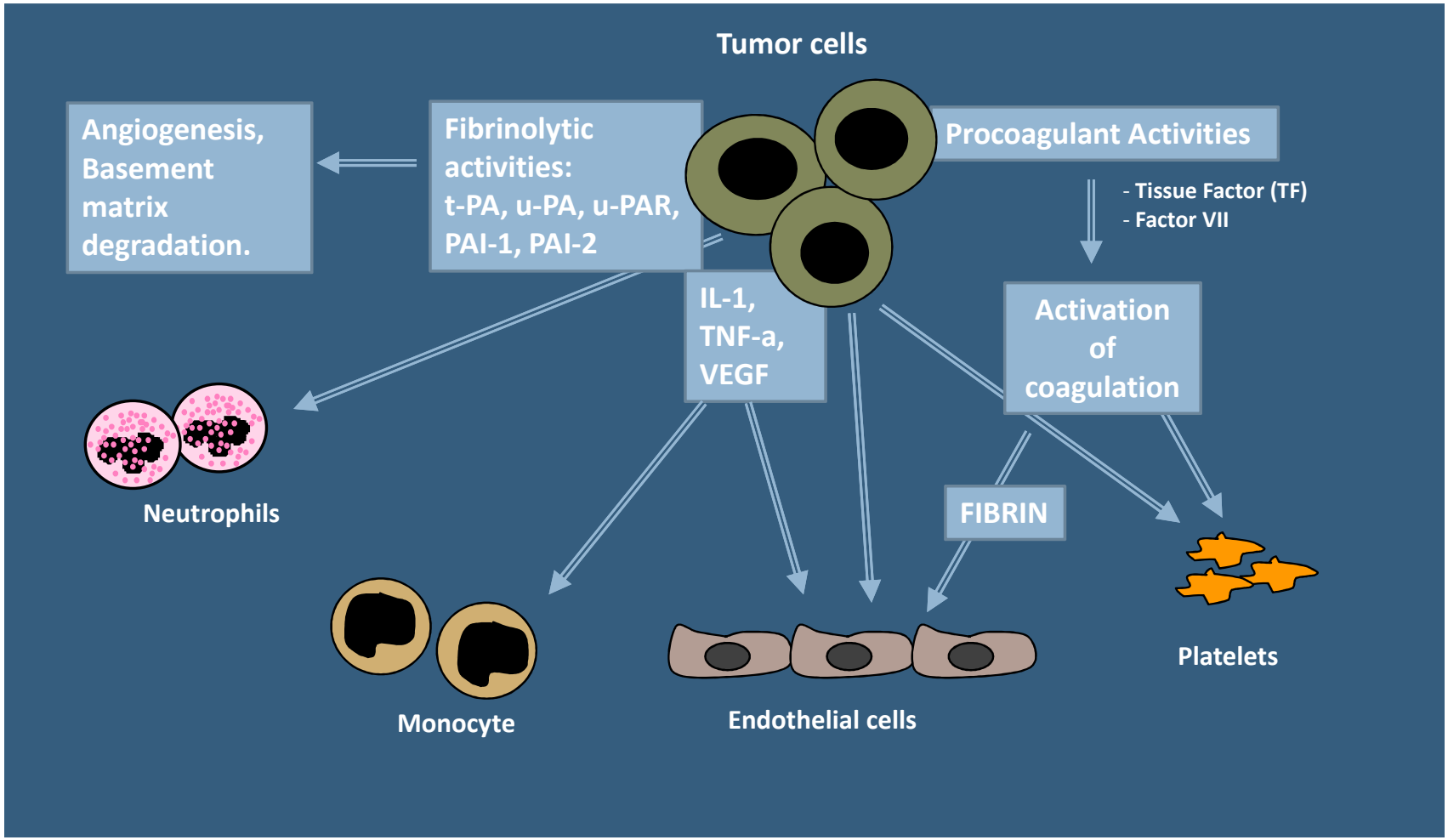
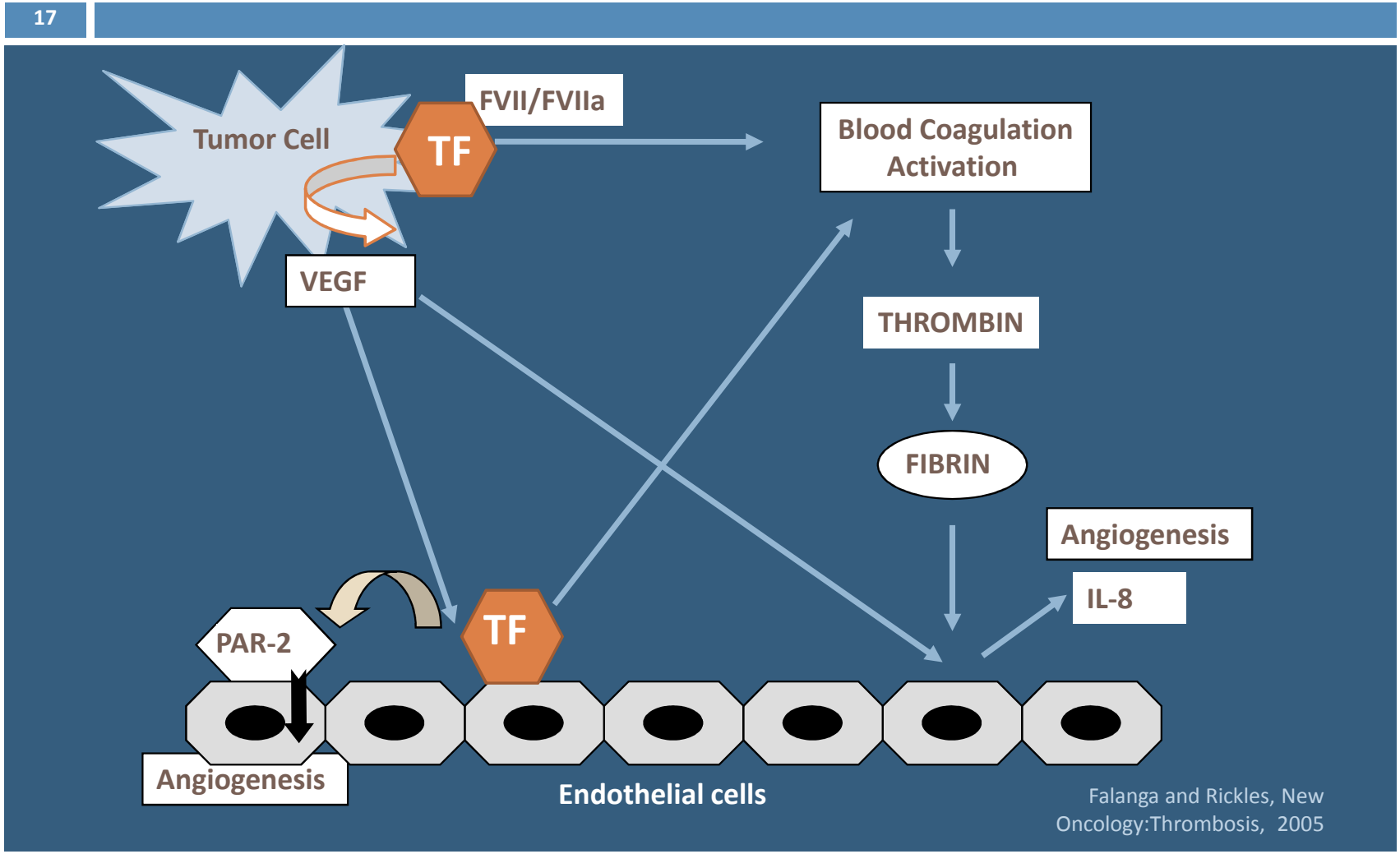
Current and future trials to test Anticoagulants to prolong survival

Interface of Tumor Biology and Hemostasis:
Thrombosis +/or Bleeding



Interface of Tumor Biology and Hemostasis:
Tumor Growth and Angiogenesis



Molecular Genetics of Thrombohemorrhagic Syndromes Associated with Human Tumors

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Oncogene tumor suppressor gene (gene products regulated)	Signaling Pathway	Tumor	Vascular outcome
MET (PAI-1; COX-2)	Tyrosine	Hepatoma kinase receptor	Thrombosis, DIC
PTEN (TF)	MEK/ERK	Glioblastoma	Thrombosis; pseudo-palisading necrosis
K-ras; p53 (TF; VEGF; TSP)	MEK/MAPK/PI3K	Colon Cancer	Angiogenesis

PAI-1 = plasminogen activator inhibitor-1; COX-2 = cyclooxygenase-2; TF = tissue factor; VEGF = vascular endothelial growth factor; TSP = thrombospondin

(Boccaccio et.al. Nature 2005;434:396; Rong et.al. Cancer Res 2005;65:1406; Yu et.al. Blood 2005;105:1734)

Molecular Genetics of Thrombohemorrhagic Syndromes Leukemia and Myeloproliferative Disease

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Disease	Gain of Function Mutation	Hemostatic Effect
APL	PML/RARa (t_{15-17})	TF (Blast cell)
ET	JAK2V617F	TF (Platelet)

APL = acute promyelocytic leukemia;
PML/RARalpha = promyelocytic leukemia/retinoic acid receptor alpha gene; TF = tissue factor;
ET = essential thrombocythemia;
JAK = Janus Kinase gene

Cheng et.al. *Proc Nat Acad Sci (USA)* 1999;96:6318; Falanga et.al. *Exp Hematol* 2007:35:702