Problemi … problemi … problemi… problemi…

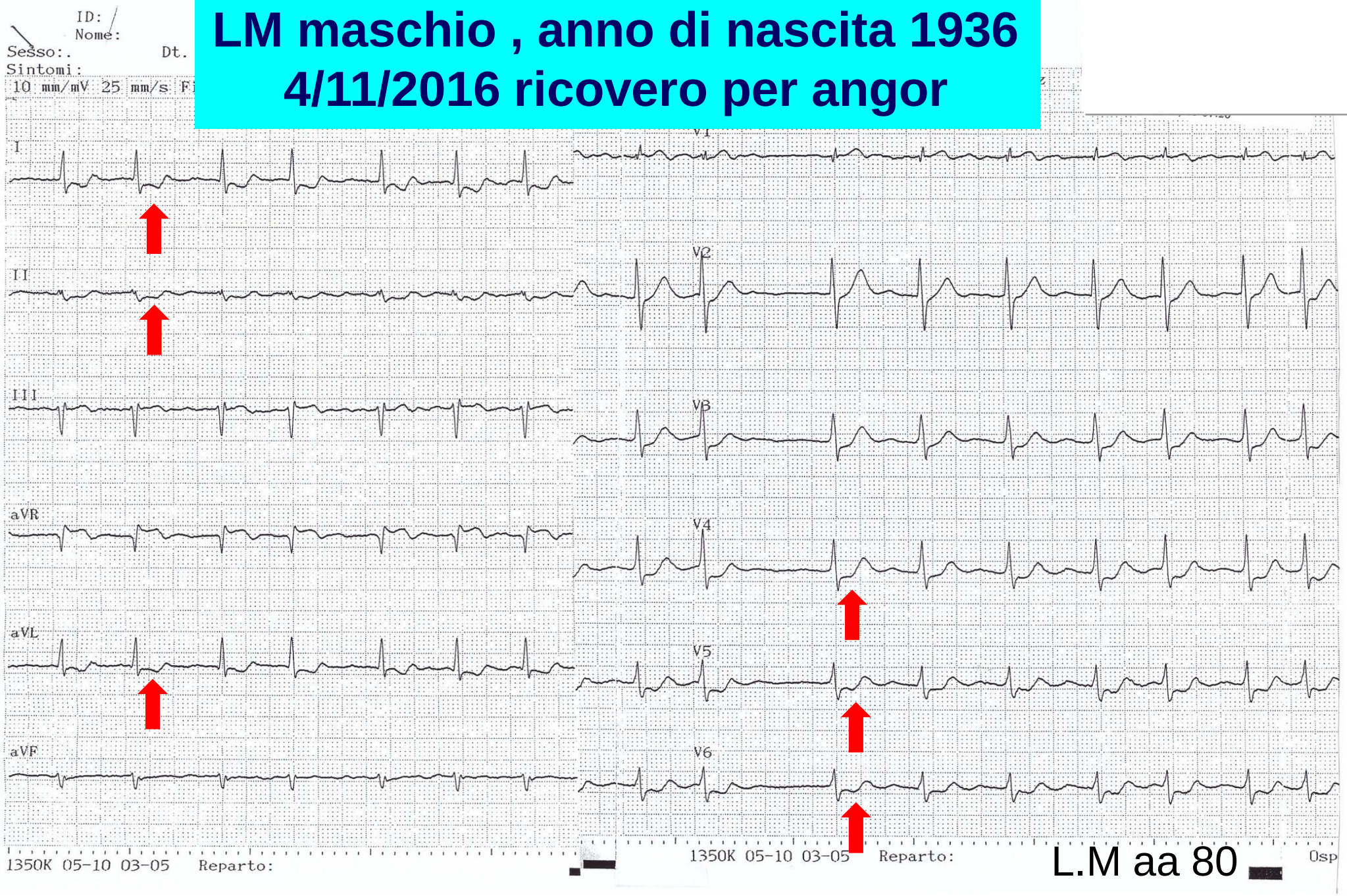
Ferdinando Maria Massari

La terapia coronaro-attiva : quali problematiche propone?

LM maschio , anno di nascita 1936

- ADENO K PROSTATICO
- 1986 Ca SPINOCELLULARE LABBRO INFERIORE
- IPERTENSIONE ARTERIOSA
- NORMALE FE (65%) , ATRIOMEGALIA SINISTRA (40 ml / m2)
- ECTASIA AORTA ADDOMINALE
- INIZIO 2015 RISCONTRO OCCASIONALE DI F.A. → APIXABAN
- 2016 DIAGNOSI DI PARKINSON TREMORIGENO

LM maschio , anno di nascita 1936
4/11/2016 ricovero per angor



L.M aa 80

713-16 - [redacted] - XA - - 04/11/2016 09:17:19

All

Key

98

Stack | Tile | Lightbox

713-16
15/08/1936 M
04/11/2016
09:17:19

Marcello

Se 1 Im 110000

Policlinico Milano
XA DFP-8000D
512 x 512 8 Bit

Zoom 111%
WC 127 WW 123

Pat. Position
45 PA 22 SA
178.555 ImgAreaDose

119.26 kV 653 mA 896 ms mAs

Reti senza fili rilevate

Sono disponibili una o più reti senza fili. Per visualizzarne un elenco e connettersi, fare clic su questo messaggio.

Viewer Toolbox 768

Standard | Special | WL

1:1

--- Film display ---

1 15 fps 30

1 frame 98

--- Image processing ---

DICOM

--- Info ---

VEPRO

EMR Viewer - VEPRO - DEMO Mode [USER]

Samsung CLX-3300 Seri...

Fullscreen

713-16 - Lochis, Marcello - XA - - 04/11/2016 09:17:19

All

Key

98 110 100 98 95 82 72 17 80 89 52 14 68 65 81 72 78

Stack Tile Lightbox

713-16
15/08/1936
04/11/2016
09:29:16

Lochis, Marcell
M

Se 5

Im 510000

Policlinico Milano
XA DFP-8000D
512 x 512 8 Bit

Zoom 169%
WC 145 WW 171

10 cm

Pat. Position
0 PA 30 SA
71.135 ImgAreaDose

96.39 kV 808 mA 760 ms mAs

IT

713-16 - [redacted] - XA - - 04/11/2016 09:27:01

All

Key

100

Stack | Tile | Lightbox

713-16
15/08/1936 M
04/11/2016
09:27:01

Marcello

Se 3 Im 310000

Policlinico Milano
XA DFP-8000D
512 x 512 8 Bit

Zoom 111%
WC 134 WW 164

10 cm

Pat. Position
-20 PA -20 SA
127.223 ImgAreaDose

82.43 kV 841 mA 737 ms mAs

Viewer Toolbox 768

Standard | Special | WL

1:1

--- Film display ---

1 15 fps 30

1 frame 100

--- Image processing ---

DICOM

--- Info ---

VEPRO

713-16 - Lochis, Marcello - XA - - 04/11/2016 09:57:04

All

Key

Stack | Tile | Lightbox

713-16
15/08/1936
04/11/2016
09:57:04

Lochis, Marcello
M

Se 12

Im 1210000

Policlinico Milano
XA DFP-8000D
512 x 512 8 Bit

Zoom 111%
WC 140 WW 169

10 cm

Pat. Position
1 PA 33 SA
30.3 ImgAreaDose

87.48 kV 891 mA 112 ms mAs

Viewer Toolbox 768

Standard | Special | WL

1:1

--- Film display ---

1 15 fps 30

1 frame 14

--- Image processing ---

DICOM

--- Info ---

VEPRO

713-16 - [redacted] - XA - - 04/11/2016 10:03:41

All

Key

Stack | Tile | Lightbox

713-16
15/08/1936 M
04/11/2016
10:03:41

Marcello

Se 18 Im 1810000

Policlinico Milano
XA DFP-8000D
512 x 512 8 Bit

Zoom 111%
WC 139 WW 162

10 cm

Pat. Position
0 PA 30 SA
80.2 ImgAreaDose

106.38 kV 732 mA 792 ms mAs

Viewer Toolbox 768

Standard | Special | WL

1:1

Film display

1 15 fps 30

1 frame 99

Image processing

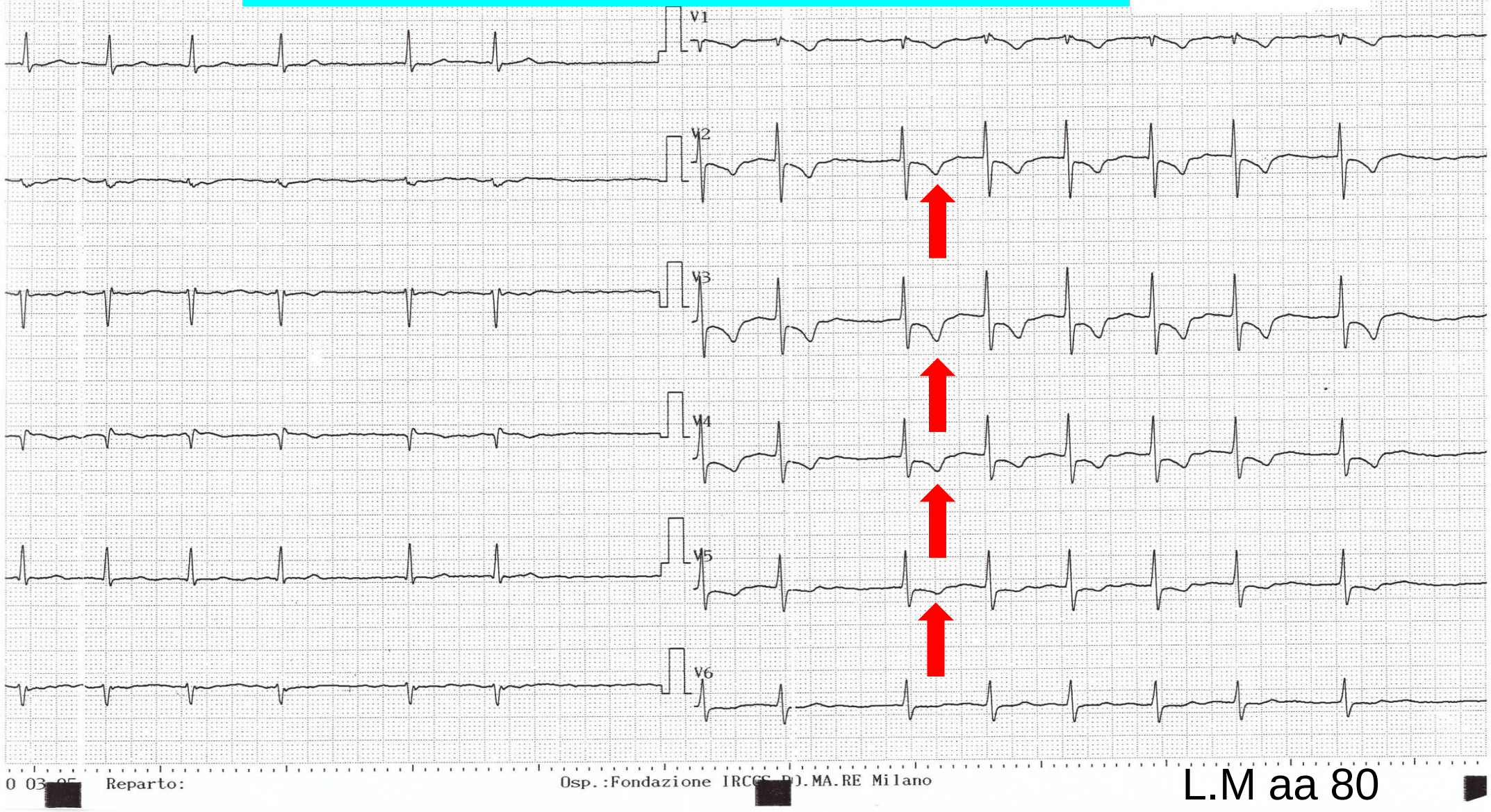
DICOM

Info

VEPRO

LM maschio , anno di nascita 1936
4/11/2016 ricovero per angor

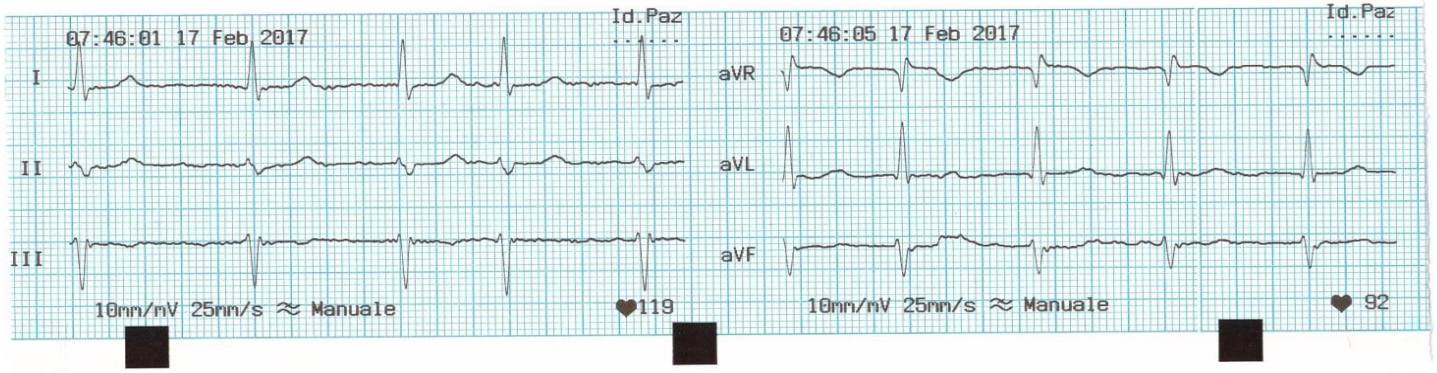
Ck mx 72
Tn hs 102 mx

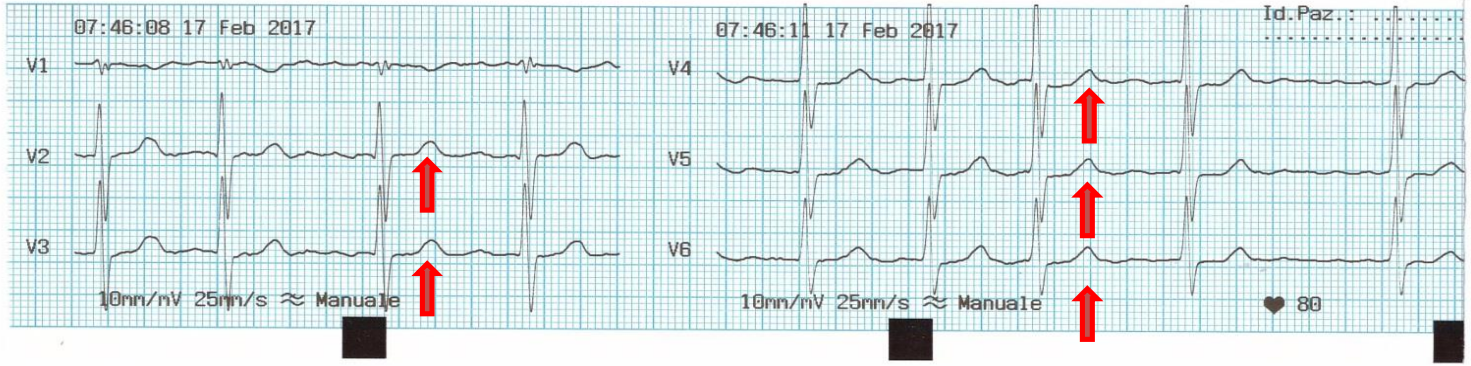


L.M aa 80

LM maschio , anno di nascita 1936

Coronaropatico con FA permanente
Controllo ambulatoriale febbraio 2017 – FE 55%





L.M aa 80

Quali problematiche propone ……

… la terapia coronaro-attiva orale

BISOPROLOLO 2,5 mg - ATORVASTATINA 40 mg - RAMIPRIL 5 mg
ASA - CLOPIDOGREL 75 mg + APIXABAN 2,5 mg x 2
PROTEZIONE GASTRICA – NITRATO S.L.

BETA BLOCCO

CONSUMO O2
FC < 70 MIN
AUMENTO DEL TEMPO DIASTOLICO DI PERFUSIONE CORONARICO
ARITMIE

ANTIAGGREGANTI

TROMBOSI CORONARICA / STENT

ACE INIBITORI

INSUFFICIENZA V.S.
IPERTENSIONE

STATINA / EZET.

IPERCOLESTE-ROLEMIA

STABILITA' DI PLACCA

Quali problematiche propone ……

… la terapia coronaro-attiva orale

BISOPROLOLO 2,5 mg – ATORVASTATINA 40 mg - RAMIPRIL 5 mg
ASA 100 mg - CLOPIDOGREL 75 mg + APIXABAN 2,5 mg x 2
PROTEZIONE GASTRICA – NITRATO S.L.

SCELTA DELLA MOLECOLA

DURATA DELLE TERAPIE

EFFETTI COLLATERALI

INTERAZIONI FARMACOLOGICHE

ADESIONE
8 farmaci X
9 somministrazioni

TOLLERABILITA’

Quali problematiche propone ……

… la terapia coronaro-attiva orale

BETA BLOCCANTE – Scelta in base alla FE ed ETA'

FE NORMALE
ETA' GIOVANE
ADULTA

→

ATENOLOLO
25-100 mg die
METOPROLOLO
25-200 mg die

FE AI LIMITI INFERIORI / DEPRESSA
PZ ANZIANO (disfunzione nodo del seno)

→

BISOPROLOLO
1,25 → 10 mg die

CARVEDILOLO
3,125 → 25 mg x 2 die

NEBIVOLOLO
1,25 → 5 mg die

→

SE FC NON RIDOTTA
MISURA OTTIMALE
e /o ipotensione

→ ASSOCIAZIONE CON IVABRADINA
5-15 mg die

Quali problematiche propone ……

… la terapia coronaro-attiva orale

BETA BLOCCANTE

ASMA

F RAYNAUD (donne, patologie autoimmuni)

→

VERAPAMIL
DILTIAZEM
IVABRADINA

BRADI ARITMIE → **BETA BLOCCO + PACE MAKER "PERSONALIZZATO"** →

FE NORMALE → PM DDD

FE DEPRESSA → PM BIVENTRICOLARE / ICD

Quali problematiche propone ……

… la terapia coronaro-attiva orale

BETA BLOCCANTE

AVVERTIRE IL PAZIENTE CIRCA LA POSSIBILITA' DI MASCHERAMENTO DEI SINTOMI DI IPOGLICEMIA

Quali problematiche propone ……

… la terapia coronaro-attiva orale

Calcio antagonisti - Ivabradina

VERAPAMIL
Sino a 240 mg die

DILTIAZEM
Sino a 300 mg die

→

BRADIARITMIE
DEPRESSIONE F.E.

STIPSI
EDEMI DECLIVI

IVABRADINA

2,5 mg x 2
Sino a
7,5 mg x 2

→

TURBE DEL VISUS
(canali If retinici)

TITOLARE LA DOSE
SPECIE
QUELLA SERALE

Quali problematiche propone ……

… la terapia coronaro-attiva orale

STATINA – DOSE INIZIALE ELEVATA - EZETIMIBE

CORONAROPATIA SEVERA , DIABETICI

MIALGIE CON O SENZA AUMENTO CK

TRANSAMINASI ELEVATE

ATORVASTATINA 40-80 mg die
ROSUVASTATINA 20-40 mg die

→

ATORVASTATINA 20 mg die

ROSUVASTATINA 5-10-20 mg die

AUTO SOSPENSIONE

“PROPOSTA” MONAKOLINA K

Quali problematiche propone ……

… la terapia coronaro-attiva orale

STATINA – DOSE INIZIALE ELEVATA - EZETIMIBE

CORONAROPATIA SEVERA , DIABETICI

MIALGIE CON O SENZA AUMENTO CK

TRANSAMINASI ELEVATE

ATORVASTATINA 40-80 mg die
ROSUVASTATINA 20-40 mg die

→

ATORVASTATINA 20-30-60 mg die

ROSUVASTATINA 5-10-20 mg die

AUTO SOSPENSIONE

“PROPOSTA” MONAKOLINA K

Quali problematiche propone ……

… la terapia coronaro-attiva orale

ACE INIBITORE / SARTANO

MONITORAGGIO FUNZIONE RENALE (SOFFI ADDOMINALI !!)

TOSSE

TITOLAZIONE DOSE SINO ALLA MASSIMA TOLLERATA

→

MONITORAGGIO P.A. EVENTUALE SOMMINISTRAZIONE SERALE

SCARSA EFFICACIA FE < 30 % → SHIFT A SACUBITRIL - VALSARTAN

Quali problematiche propone ……

… la terapia coronaro-attiva orale

ACE INIBITORE / SARTANO

MONITORAGGIO FUNZIONE RENALE (SOFFI ADDOMINALI !!)

TOSSE

TITOLAZIONE DOSE SINO ALLA MASSIMA TOLLERATA

MONITORAGGIO P.A. EVENTUALE SOMMINISTRAZIONE SERALE

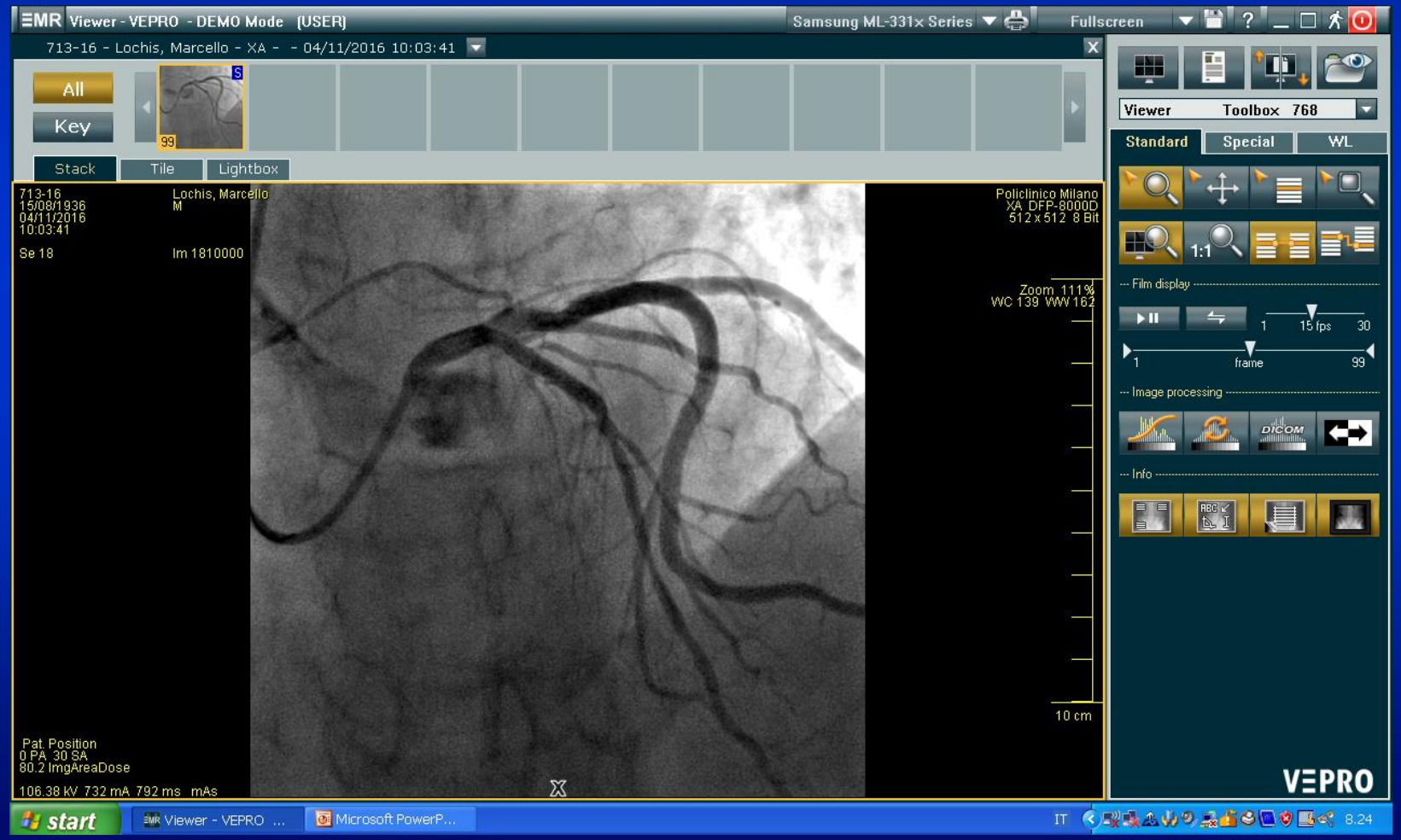
SCARSA EFFICACIA FE < 30 % → SHIFT A SACUBITRILVALSARTAN

Piu' stretto monitoraggio funzione renale ed elettroliti
Ipotensione
Riduzione diuretico

Quali problematiche propone ……

… la terapia coronaro-attiva orale

DOPPIA ANTIAGGREGAZIONE (+ TAO)



Quali problematiche propone ……

… la terapia coronaro-attiva orale

DOPPIA ANTIAGGREGAZIONE (+ TAO)

SANGUINAMENTO
TOLLERABILITA'
GASTRICA

PROCEDURE
CHIRURGICHE
Spt ODONTOIATRICHE

No eparina s.c. al posto della terapia anti aggregante !!!!

Organo Ufficiale di
Federazione Italiana di Cardiologia FIC

Società Italiana di Chirurgia Cardiaca

STENT CORONARICO E CHIRURGIA

Adattato da G Ital Cardiol 2012;13(7-8):525-551
www.giornaledicardiologia.it

La gestione perioperatoria della terapia antiaggregante nel paziente portatore di stent coronarico candidato a intervento chirurgico

versione tascabile

Allegato al Giornale Italiano di Cardiologia Vol. 13 | Numero 7-8 | Luglio-Agosto 2012

Il Pensiero Scientifico Editore

In odontoiatria

Tabella 12. Odontoiatria.

Rischio emorragico	Rischio trombotico: Basso	Rischio trombotico: Intermedio	Rischio trombotico: Alto
Basso Terapia parodontale non chirurgica (inclusa ablazione del tartaro) Terapia endodontica non chirurgica Posizionamento della diga di gomma	prosegue	prosegue	prosegue
Intermedio Terapia parodontale chirurgica (chirurgia resettiva, chirurgia rigenerativa, chirurgia mucogengivale) Chirurgia orale in genere (chirurgia estrattiva, chirurgia ricostruttiva preimplantare) Chirurgia implantare	prosegue	prosegue	prosegue
Alto Nessuno			

ASA, aspirina.

Quali problematiche propone ……

… la terapia coronaro-attiva orale

DOPPIA ANTIAGGREGAZIONE (+ TAO)

SANGUINAMENTO TOLLERABILITA' GASTRICA

PROCEDURE CHIRURGICHE Spt ODONTOIATRICHE

ASSOCIAZIONE CON DICUMAROLICI / DOAC IN PZ CON F.A. / VALVOLARI OPERATI

SCELTA DELLO STENT E PRECISE INDICAZIONI IN LETTERA

ESC European Society of Cardiology
European Heart Journal (2019) 00, 1–71
doi:10.1093/eurheartj/ehz425
ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)

Antithrombotic therapy in post-PCI patients with AF or another indication for an OAC		
It is recommended that peri-procedural aspirin and clopidogrel are administered to patients undergoing coronary stent implantation.	I	C
In patients who are eligible for a NOAC, it is recommended that a NOAC (apixaban 5 mg b.i.d., dabigatran 150 mg b.i.d., edoxaban 60 mg o.d., or rivaroxaban 20 mg o.d.)[f] is used in preference to a VKA in combination with antiplatelet therapy.[300,301,308,310,311]	I	A
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and an OAC.	III	C
Dual therapy with an OAC and either ticagrelor or prasugrel may be considered as an alternative to triple therapy with an OAC, aspirin, and clopidogrel in patients with a moderate or high risk of stent thrombosis,[h] irrespective of the type of stent used.	IIb	C

ESC European Society of Cardiology
European Heart Journal (2019) 00, 1–71
doi:10.1093/eurheartj/ehz425
ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)

After uncomplicated PCI, early cessation (≤1 week) of aspirin and continuation of dual therapy with an OAC and clopidogrel should be considered if the risk of stent thrombosis[h] is low, or if concerns about bleeding risk prevail over concerns about the risk of stent thrombosis,[h] irrespective of the type of stent used.[301,308–310]	IIa	B
Triple therapy with aspirin, clopidogrel, and an OAC for ≥1 month should be considered when the risk of stent thrombosis[h] outweighs the bleeding risk, with the total duration (≤6 months) decided according to assessment of these risks and clearly specified at hospital discharge.	IIa	C
In patients with an indication for a VKA in combination with aspirin and/or clopidogrel, the dose intensity of the VKA should be carefully regulated with a target international normalized ratio in the range of 2.0–2.5 and with time in therapeutic range >70%.[300,301,308–310]	IIa	B

Use of proton pump inhibitors		
Concomitant use of a proton pump inhibitor is recommended in patients receiving aspirin monotherapy, DAPT, or OAC monotherapy who are at high risk of gastrointestinal bleeding.[284]	I	A

DOPPIA ANTIAGGREGAZIONE +/- DOAC - VKA

TIPOLOGIA DI STENT

RISCHIO EMORRAGICO

RISCHIO ISCHEMICO

DOPO ACS

LETTERA DI DIMISSIONE

ESC European Society of Cardiology
European Heart Journal (2019) **00**, 1–71
doi:10.1093/eurheartj/ehz425
ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)

Quali Doac ?

When rivaroxaban is used and concerns about high bleeding risk[d] prevail over concerns about stent thrombosis[h] or ischaemic stroke,[g] rivaroxaban 15 mg o.d. should be considered in preference to rivaroxaban 20 mg o.d. for the duration of concomitant single or dual antiplatelet therapy.[300,301,308,310]	IIa	B
When dabigatran is used and concerns about high bleeding risk[d] prevail over concerns about stent thrombosis[h] or ischaemic stroke,[g] dabigatran 110 mg b.i.d. should be considered in preference to dabigatran 150 mg b.i.d. for the duration of concomitant single or dual antiplatelet therapy.[300,301,308]	IIa	B

ORIGINAL ARTICLE

Antithrombotic Therapy after Acute Coronary Syndrome or PCI in Atrial Fibrillation

Renato D. Lopes, M.D., Ph.D., Gretchen Heizer, M.S., Ronald Aronson, M.D., Amit N. Vora, M.D., M.P.H., Tyler Massaro, Ph.D., Roxana Mehran, M.D., Shaun G. Goodman, M.D., Stephan Windecker, M.D., Harald Darius, M.D., Jia Li, Ph.D., Oleg Averkov, M.D., Ph.D., M. Cecilia Bahit, M.D., Otavio Berwanger, M.D., Ph.D., Andrzej Budaj, M.D., Ph.D., Ziad Hijazi, M.D., Ph.D., Alexander Parkhomenko, M.D., Ph.D., Peter Sinnaeve, M.D., Ph.D., Robert F. Storey, M.D., Holger Thiele, M.D., Dragos Vinereanu, M.D., Ph.D., Christopher B. Granger, M.D., and John H. Alexander, M.D., M.H.S., for the AUGUSTUS Investigators*

ABSTRACT

BACKGROUND

Appropriate antithrombotic regimens for patients with atrial fibrillation who have an acute coronary syndrome or have undergone percutaneous coronary intervention (PCI) are unclear.

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Lopes at the Duke Clinical Research Institute, 200 Morris St., Durham, NC

Conclusions

In patients with atrial fibrillation and a recent acute coronary syndrome or PCI treated with a $P2Y_{12}$ inhibitor, an antithrombotic regimen that included apixaban, without aspirin, resulted in less bleeding and fewer hospitalizations without significant differences in the incidence of ischemic events than regimens that included a vitamin K antagonist, aspirin, or both.

(N.Engl. J.Med. 2019; 380: 1509-24)

The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

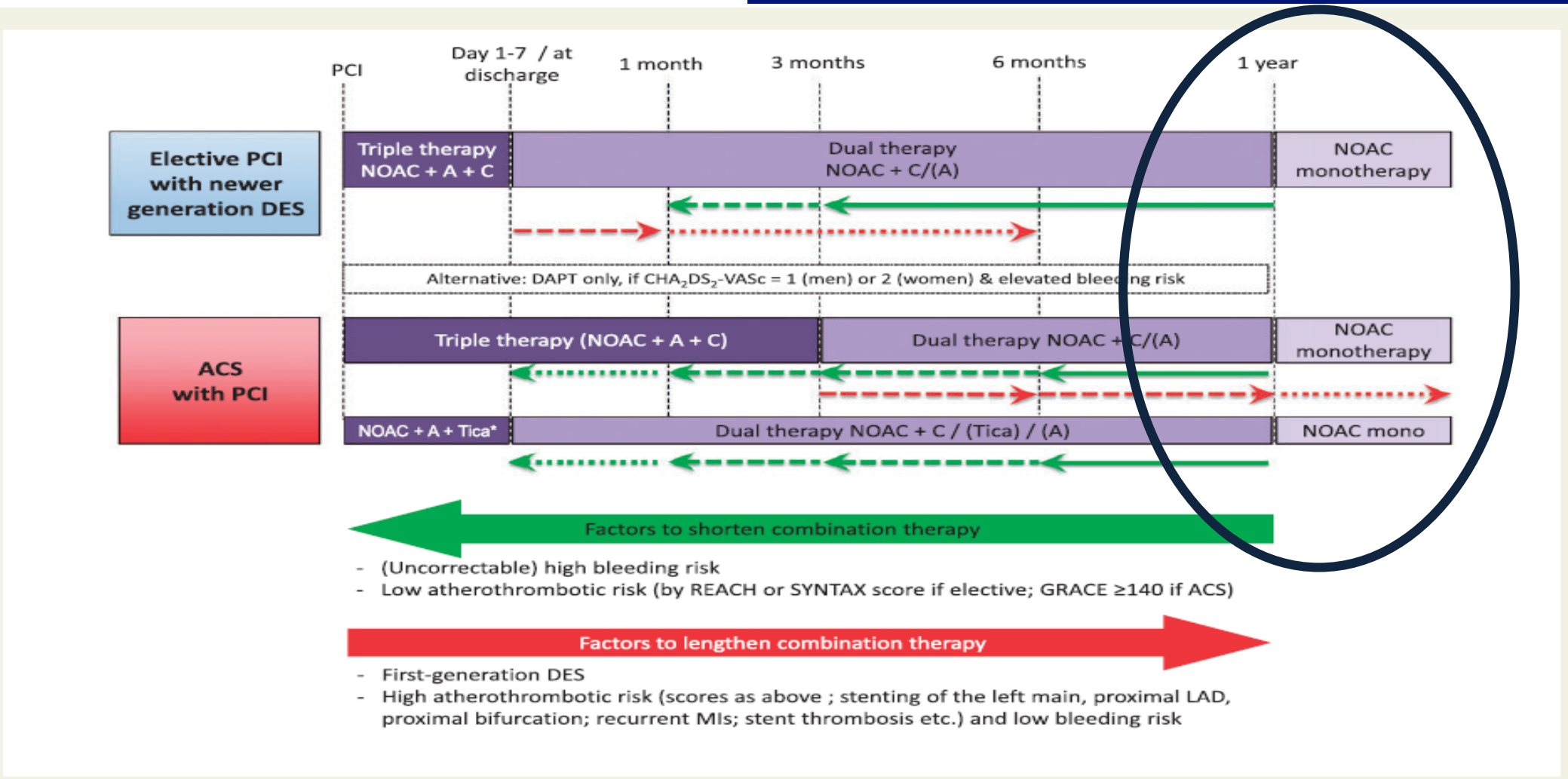


Figure 11 Long-term treatment of patients on non-vitamin K antagonist oral anticoagulant therapy after elective percutaneous coronary intervention or acute coronary syndrome. There are innumerable possible variations on this global theme, as discussed in the text. Patient characteristics and institutional practices should be taken into account to *individualize the approach* to each and every single patient. This figure wants to create a 'backbone' as guidance for such tailored approaches. A: aspirin 75–100 mg OD; C: clopidogrel 75 mg OD; Tica: Ticagrelor 90 mg BID. *If triple therapy needs to be continued after discharge clopidogrel is preferred over ticagrelor (due to lack of data).

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 19, 2019 VOL. 381 NO. 12

Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease

Satoshi Yasuda, M.D., Ph.D., Koichi Kaikita, M.D., Ph.D., Masaharu Akao, M.D., Ph.D., Junya Ako, M.D., Ph.D., Tetsuya Matoba, M.D., Ph.D., Masato Nakamura, M.D., Ph.D., Katsumi Miyauchi, M.D., Ph.D., Nobuhisa Hagiwara, M.D., Ph.D., Kazuo Kimura, M.D., Ph.D., Atsushi Hirayama, M.D., Ph.D., Kunihiko Matsui, M.D., M.P.H., and Hisao Ogawa, M.D., Ph.D., for the AFIRE Investigators*

ABSTRACT

BACKGROUND

Conclusions

As antithrombotic therapy, rivaroxaban monotherapy was non inferior to combination therapy for efficacy and superior for safety in patients with atrial fibrillation and stable coronary artery disease (N.Engl. J.Med. 2019; 381: 1103-13)

LM maschio , anno di nascita 1936

- ADENO K PROSTATICO
- 1986 Ca SPINOCELLULARE LABBRO INFERIORE
- IPERTENSIONE ARTERIOSA
- NORMALE FE (65%) , ATRIOMEGALIA SINISTRA (40 ml / m2)
- ECTASIA AORTA ADDOMINALE
- **INIZIO 2015 RISCONTRO OCCASIONALE DI F.A.**
- 2016 DIAGNOSI DI PARKINSON TREMORIGENO

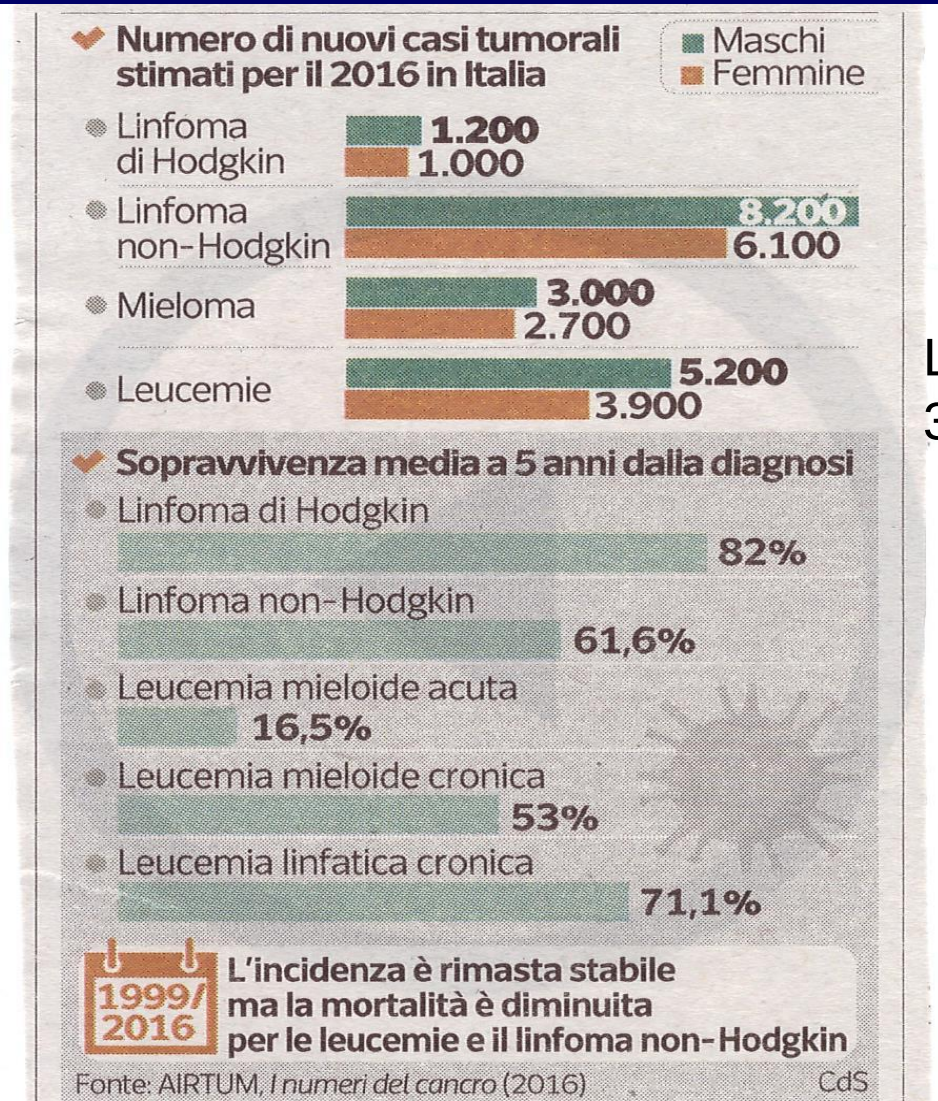
LM maschio , anno di nascita 1936

- **Leucemia Linfocitica Cronica diagnosticata nel 2002**
  (linfoadenopatie, splenomegalia e aumento della conta linfocitaria)

LM maschio , anno di nascita 1936

Leucemia Linfocitica Cronica diagnosticata nel 2002

(linfoadenopatie, splenomegalia e aumento della conta linfocitaria)



LLC
30% delle leucemie

LM maschio , anno di nascita 1936

- **Leucemia Linfocitica Cronica diagnosticata nel 2002 (linfoadenopatie, splenomegalia e aumento della conta linfocitaria)**
- **Fludarabina (** nucleotide fluorurato idrosolubile, analogo dell'agente antivirale vidarabina) → **anemia emolitica**
- **Nel 2007 → prognosi inferiore a 6 mesi → alemtuzumab → anemia emolitica**
- **2010 steroide e rituximab (** anticorpo monoclonale chimerico murino/umano ottenuto con tecniche di ingegneria genetica) → **mancata risposta sulle masse di malattia**
- **2012 bendamustina (agente alchilante / antimetabolita analogo della purina) e rituximab**
- **Per progressione di malattia il 20/10/2014 inizia ibrutinib**

- **Ibrutinib (PCI-32765): Ibrutinib è stato il primo inibitore di chinasi approvato dalla FDA (a febbraio 2014) per la LLC (Lamanna N et al, 2016). E' un inibitore orale irreversibile della *Bruton Tyrosine Kinase* (BTK) – proteina che agisce a valle del *B-cell Receptor* (BCR) – e della *IL-2-inducible Kinase* (ITK) (Giridhar KV et al, 2017). L'inibizione di ITK attenua le risposte Th2 a seguito della stimolazione del *T-cell Receptor*.**

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ORIGINAL ARTICLE FREE PREVIEW

Ibrutinib Regimens versus Chemoimmunotherapy in Older Patients with Untreated CLL

Jennifer A. Woyach, M.D., Amy S. Ruppert, Ph.D., Nyla A. Heerema, Ph.D., Weiqiang Zhao, M.D., Allison M. Booth, M.S., Wei Ding, M.B., B.S., Ph.D., Nancy L. Bartlett, M.D., Danielle M. Brander, M.D., Paul M. Barr, M.D., Kerry A. Rogers, M.D., Sameer A. Parikh, M.B., B.S., Steven Coutre, M.D., et al.

N Engl J Med 2018; 379:2517-2528

Abstract

Background

Ibrutinib has been approved by the Food and Drug Administration for the treatment of patients with untreated chronic lymphocytic leukemia (CLL) since 2016 but has not been compared with chemo immunotherapy.

We conducted a phase 3 trial to evaluate the efficacy of ibrutinib, either alone or in combination with rituximab, relative to chemo- immunotherapy.

F.A. (grado 3 - 4) 17/180 pz nel gruppo Ibrutinib Vs 5/176 e 10/181

Conclusions

Among older patients with untreated CLL, treatment with ibrutinib was superior to treatment with bendamustine plus rituximab with regard to progression-free survival. There was no significant difference between ibrutinib and ibrutinib plus rituximab with regard to progression-free survival.

IL PROBLEMA … ARITMIE

Table 8 Cancer drug agents associated with cardiac arrhythmias

Type of arrhythmia	Causative drug
Bradycardia	Arsenic trioxide, bortezomib, capecitabine, cisplatin, cyclophosphamide, doxorubicine, epirubicine, 5-FU, ifosfamide, IL-2, methotrexate, mitoxantrone, paclitaxel, rituximab, thalidomide.
Sinus tachycardia	Anthracyclines, carmustine.
Atrioventricular block	Anthracyclines, arsenic trioxide, bortezomib, cyclophosphamide, 5-FU, mitoxantrone, rituximab, taxanes, thalidomide.
Conduction disturbances	Anthracyclines, cisplatin, 5-FU, imatinib, taxanes.
Atrial fibrillation	Alkylating agents (cisplatin, cyclophosphamide, ifosfamide, melphalan), anthracyclines, antimetabolites (capecitabine, 5-FU, gemcitabine), IL-2, interferons, rituximab, romidepsin, small molecule TKIs (ponatinib, sorafenib, sunitinib, ibrutinib), topoisomerase II inhibitors (amsacrine, etoposide), taxanes, vinca alkaloids.
Supraventricular tachycardias	Alkylating agents (cisplatin, cyclophosphamide, ifosfamide, melphalan), amsacrine, anthracyclines, antimetabolites (capecitabine, 5-FU, methotrexate), bortezomib, doxorubicin, IL-2, interferons, paclitaxel, ponatinib, romidepsin.
Ventricular tachycardia/fibrillation	Alkylating agents (cisplatin, cyclophosphamide, ifosfamide), amsacrine, antimetabolites (capecitabine, 5-FU, gemcitabine), arsenic trioxide, doxorubicin, interferons, IL-2, methothrexate, paclitaxel, proteasome inhibitors (bortezomib, carfilzomib), rituximab, romidepsin.
Sudden cardiac death	Anthracyclines (reported as very rare), arsenic trioxide (secondary to torsade de pointes), 5-FU (probably related to ischaemia and coronary spasm), interferons, nilotinib, romidepsin.

5-FU = 5-fluorouracil; IL-2 = interleukin 2; TKI = tyrosine kinase inhibitor.

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines

Ibrutinib : inibitore della TKIs

Tabella 1: Reazioni avverse riportate negli studi clinici o durante la sorveglianza post-marketing nei pazienti con tumori delle cellule-B†

Classificazione per sistemi e organi	Frequenza (Tutti i gradi)	Reazioni avverse	Tutti i gradi (%)	Grado ≥ 3 (%)
Patologie cardiache	Comune	Fibrillazione atriale	6	3
		Tachiaritmia ventricolare*b	1	0
Patologie vascolari	Molto comune	Emorragia*#	30	1
		Ecchimosi*	22	< 1
	Comune	Ematoma subdurale#	1	1
		Epistassi	8	< 1
		Petecchie	7	0
		Ipertensione*	10	4

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Cardiovascular Toxic Effects of Targeted Cancer Therapies

Javid J. Moslehi, M.D.

N Engl J Med 2016; 375:1457-1467

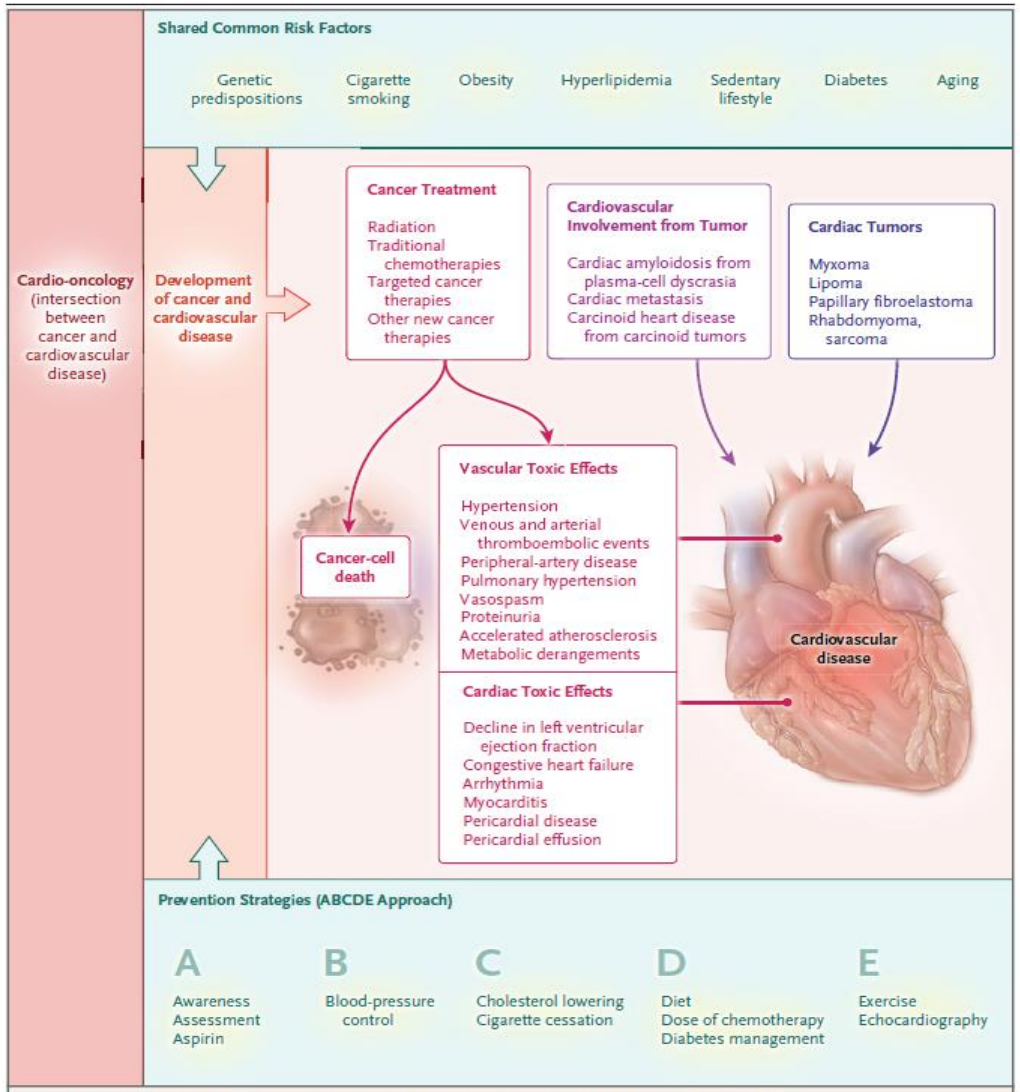
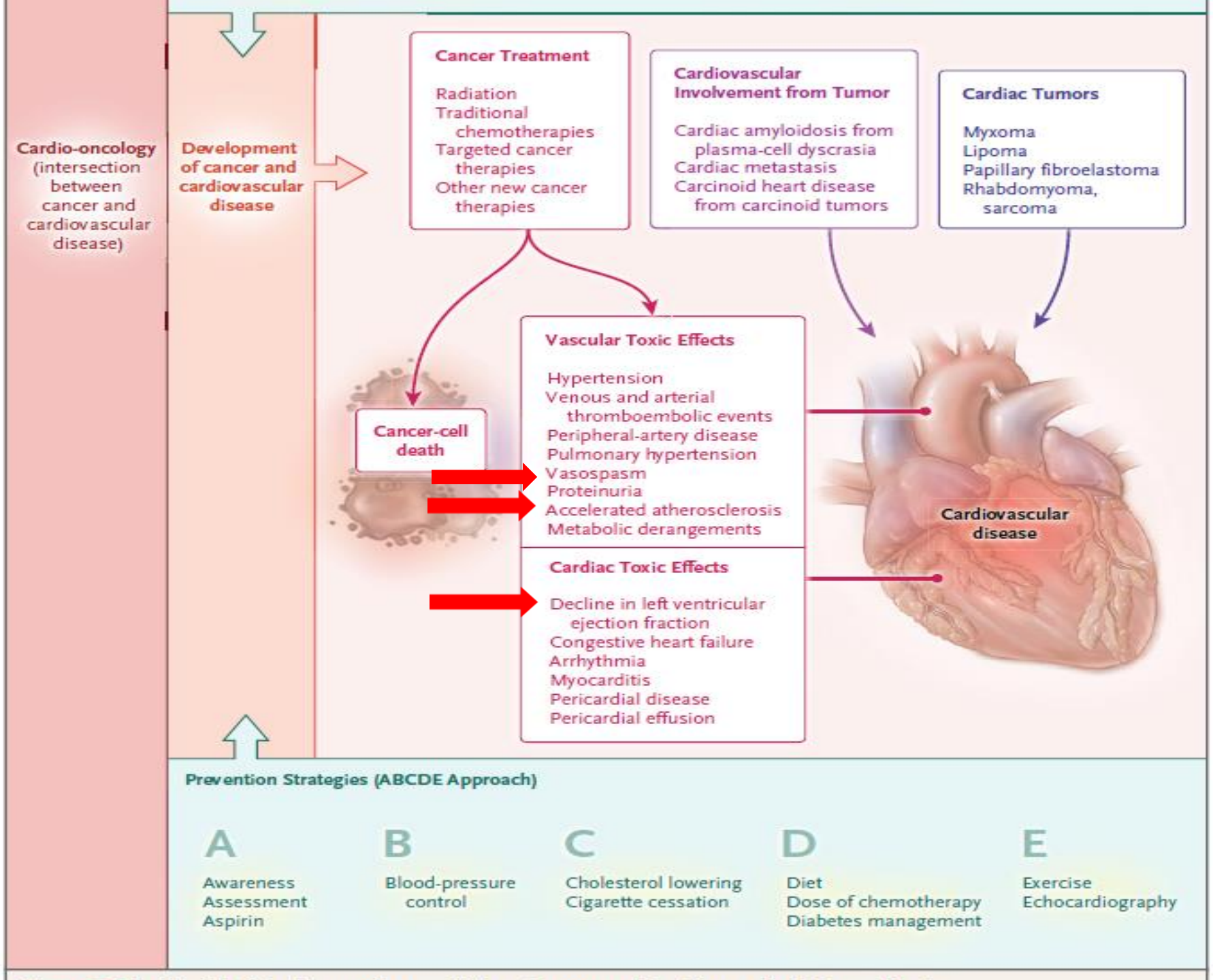


Figure 2. The World of Cardio-oncology — Where Cancer and Cardiovascular Disease Meet.
The intersection between cancer and cardiovascular disease extends beyond cardiovascular and cardiometabolic toxic effects that are associated with cancer treatment. Cancers themselves may arise from cardiac tissue or directly cause cardiovascular diseases. In addition, there is a growing appreciation of common risk factors that predispose patients to both cancer and cardiovascular disease, which are by far the two most common causes of death and complications in industrialized countries. This latter concept may have major implications for public health, including the health of more than 15 million cancer survivors in the United States alone. A simple "ABCDE" approach, which has been proposed to prevent cardiovascular disease in cancer survivors, may have the added benefit of protecting patients from the recurrence of cancer.


Cardio-oncology (intersection between cancer and cardiovascular disease)
Development of cancer and cardiovascular disease
Cancer Treatment
Radiation
Traditional chemotherapies
Targeted cancer therapies
Other new cancer therapies
Cardiovascular Involvement from Tumor
Cardiac amyloidosis from plasma-cell dyscrasia
Cardiac metastasis
Carcinoid heart disease from carcinoid tumors
Cardiac Tumors
Myxoma
Lipoma
Papillary fibroelastoma
Rhabdomyoma, sarcoma
Cancer-cell death
Vascular Toxic Effects
Hypertension
Venous and arterial thromboembolic events
Peripheral-artery disease
Pulmonary hypertension
Vasospasm
Proteinuria
Accelerated atherosclerosis
Metabolic derangements
Cardiac Toxic Effects
Decline in left ventricular ejection fraction
Congestive heart failure
Arrhythmia
Myocarditis
Pericardial disease
Pericardial effusion
Cardiovascular disease
Prevention Strategies (ABCDE Approach)
A
Awareness
Assessment
Aspirin
B
Blood-pressure control
C
Cholesterol lowering
Cigarette cessation
D
Diet
Dose of chemotherapy
Diabetes management
E
Exercise
Echocardiography

LM maschio , anno di nascita 1936

- **Leucemia Linfocitica Cronica diagnosticata nel 2002**
  (linfoadenopatie, splenomegalia e aumento della conta linfocitaria)

- **Per progressione di malattia il 20/10/2014**

inizia ibrutinib

TACHI ARITMIE

CORONARO VASCULO PATIA

INSUFFICIENZA CARDIACA

LM maschio , anno di nascita 1936

LLC DIAGNOSTICATA NEL 2002

TERAPIA in cronico : **ASA 100 mg , APIXABAN 5 mg X 2** ,
bisoprololo 2,5 mg , ramipril 5 mg,
atorvastatina 40 mg, nitrato s.l. , pantoprazolo 20 mg,
allopurinolo 300 mg , folina, pramipexolo RP 0,52 mg

Ibrutinib 140 mg 3 cp die ripreso dopo 3 settimane

QUALI PROBLEMATICHE ?

SCELTA DEL FARMACO

DURATA DELLE TERAPIE

EFFETTI COLLATERALI

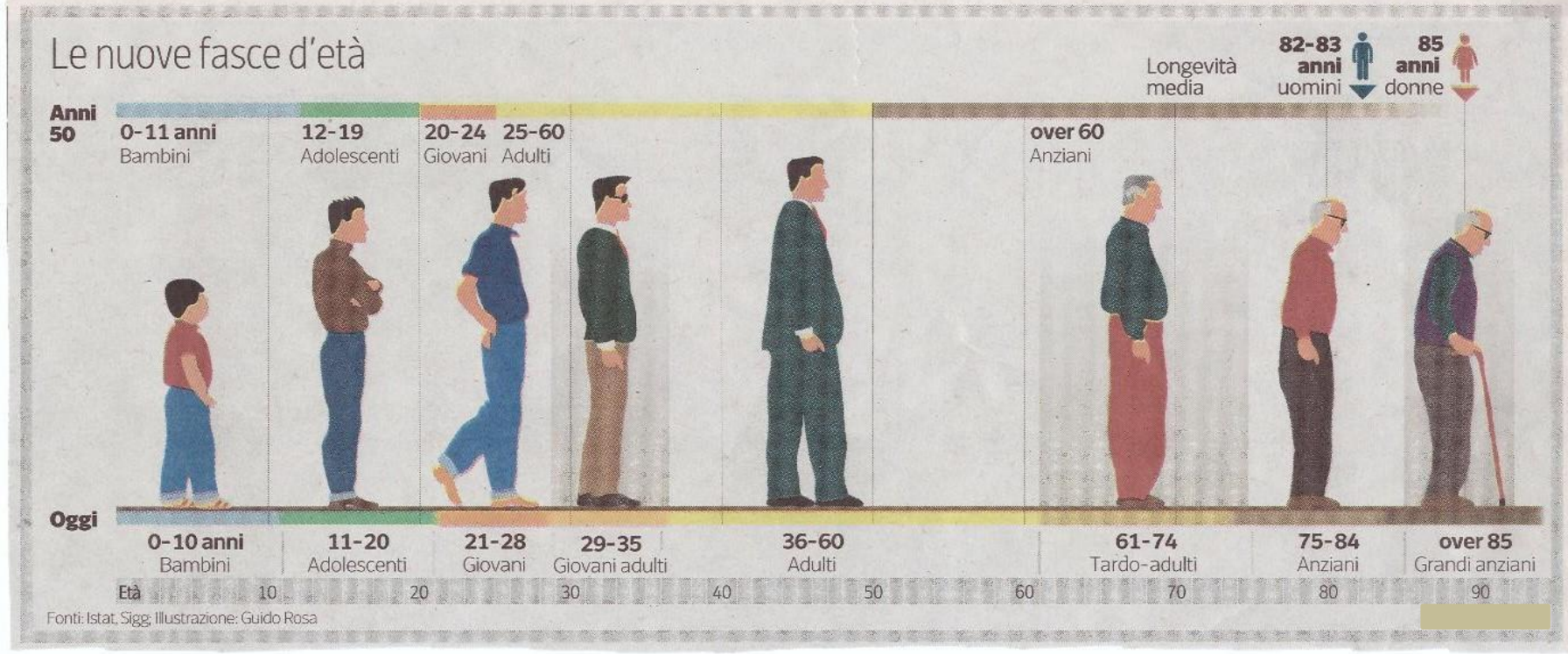
INTERAZIONI FARMACOLOGICHE

ADESIONE
11 farmaci X
13 somministrazioni

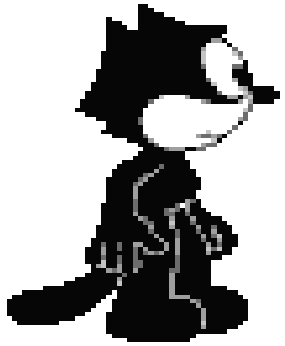
TOLLERABILITA'

Anziani? Solo dopo i 75 anni (abbiamo imparato a volerci bene)

In 12 anni ne abbiamo guadagnati 3 di vita. Le relazioni sociali da riorganizzare



Problemi … problemi … problemi… problemi…



XXIX CONGRESSO NAZIONALE ANCE

10 - 13 Ottobre 2019
Centro Congressi Hilton
Sorrento Palace Sorrento (NA)

Grazie