fondazione GIMEMA onlus
per la promozione e lo sviluppo della ricerca scientifica sulle malattie ematologiche. FRANCO MANDELLI

Dalle linee guida alla qualità di vita e alle cure palliative precoci e simultanee:

come la storia delle leucemie mieloidi acute sta cambiando

Roma, 2 febbraio 2024 – Starhotels Metropole

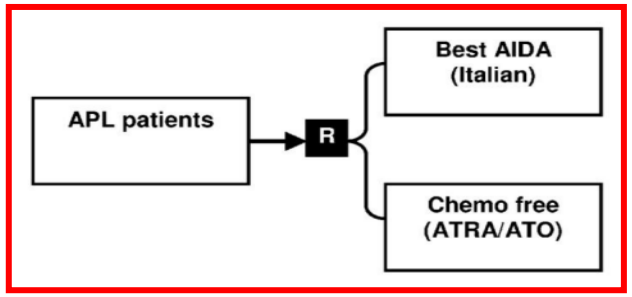
The Value of International Collaboration in Quality of Life (QoL) research in AML

Ian Thomas, Research Fellow
Cardiff University

- What we do in UK AML trials, and how
- What we plan to do in the future
- How we want to collaborate internationally

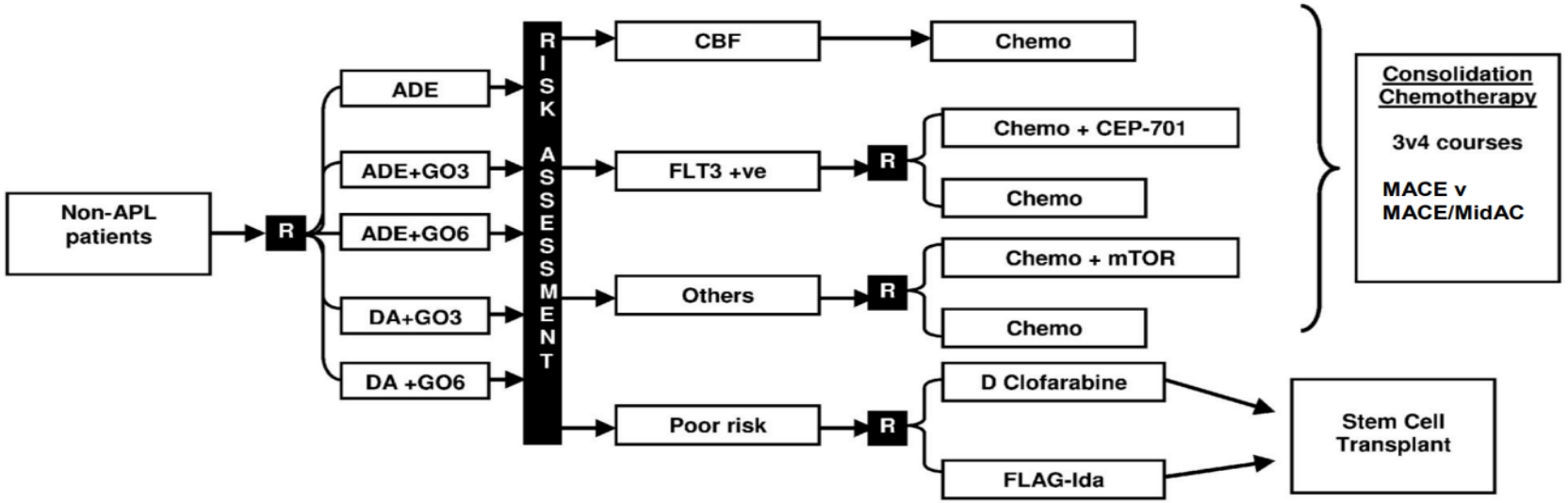
WORKING PARTIES ON LEUKAEMIA IN ADULTS AND CHILDREN TRIAL IN ACUTE MYELOID LEUKAEMIA OR HIGH RISK 17 AML17

Flow chart for adult patients



Arsenic trioxide and all-*trans* retinoic acid treatment for acute promyelocytic leukaemia in all risk groups (AML17): results of a randomised, controlled, phase 3 trial

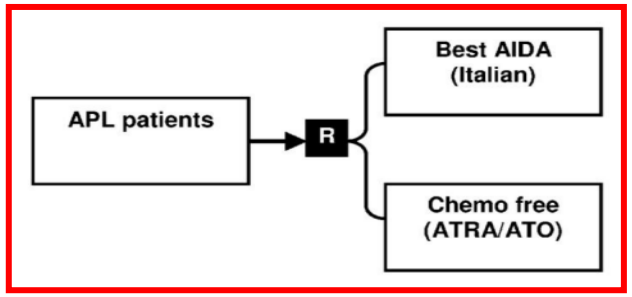
Alan K Burnett, Nigel H Russell, Robert K Hills, David Bowen, Jonathan Kell, Steve Knapper, Yvonne G Morgan, Jennie Lok, Angela Grech, Gail Jones, Asim Khwaja, Lone Friis, Mary Frances McMullin, Ann Hunter, Richard E Clark, David Grimwade, for the UK National Cancer Research Institute Acute Myeloid Leukaemia Working Group

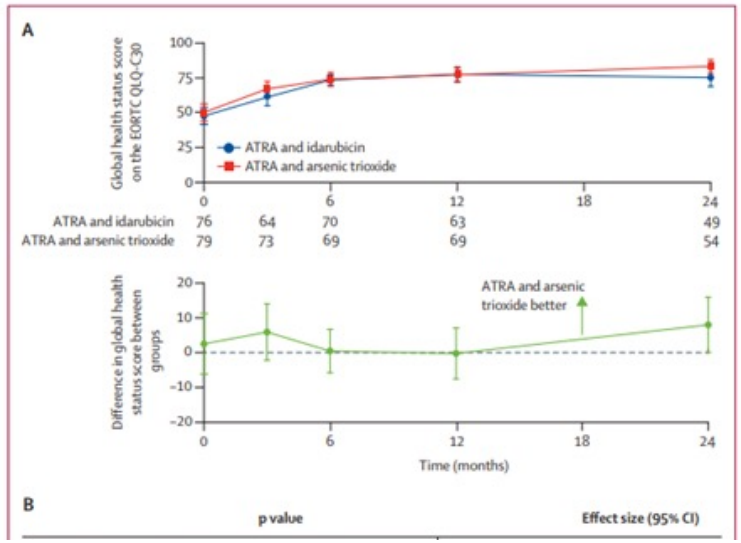


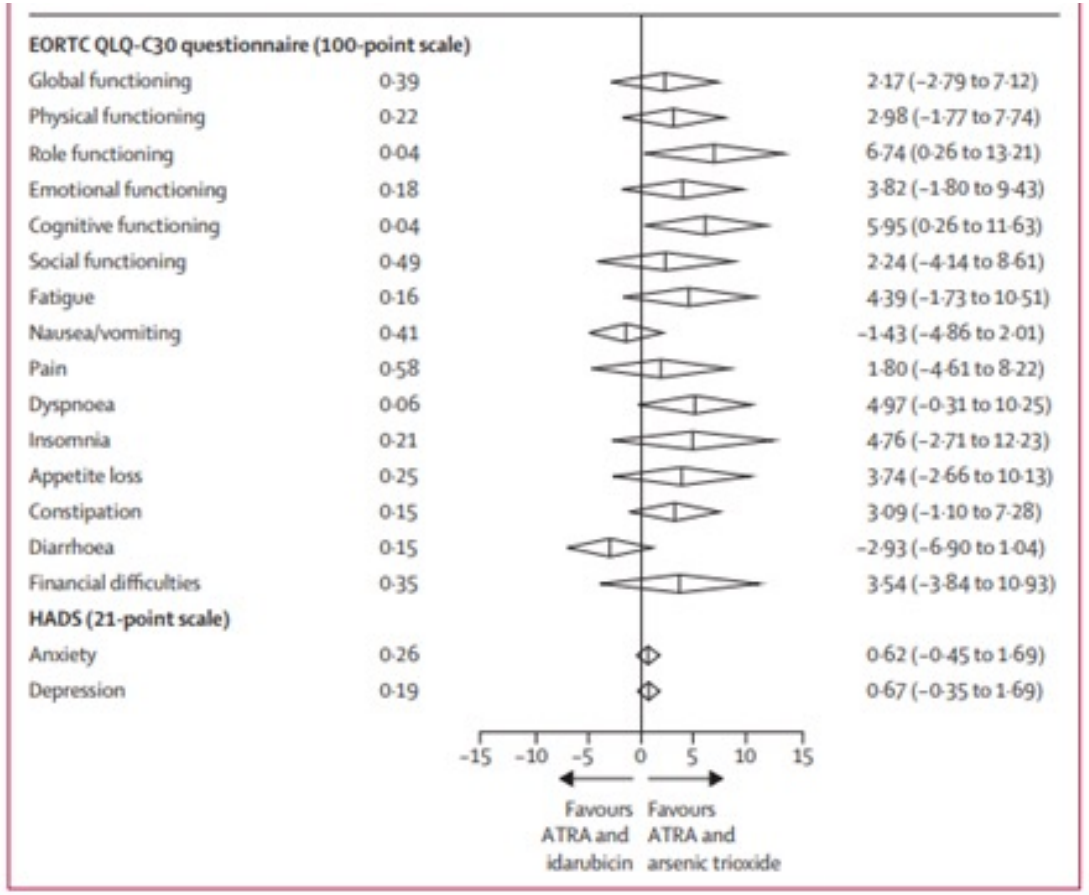
Version 3.2: May 2009

WORKING PARTIES ON LEUKAEMIA IN ADULTS AND CHILDREN TRIAL IN ACUTE MYELOID LEUKAEMIA OR HIGH RISK 17 AML17

Flow chart for adult patients







Combining or meta-analyzing data

Clinical evidence

The clinical-effectiveness evidence is relevant to NHS clinical practice in England

3.5 The evidence for arsenic trioxide in untreated acute promyelocytic leukaemia came from 2 clinical trials: APL0406 (n=266) and AML17 (n=235). Both studies were phase III, randomised, open-label trials; only AML17 included patients from the UK. Both trials compared arsenic trioxide plus ATRA with AIDA. The committee understood that APL0406 used the dosing schedule and population defined in the marketing authorisation for arsenic trioxide, whereas AML17 used a lower dose (about 60% of that in the marketing authorisation) and included people with high-risk disease. The clinical expert confirmed that in England, arsenic trioxide has been used according to the AML17 protocol. However, the committee agreed that it could only appraise arsenic trioxide within its marketing authorisation. The ERG highlighted that the populations in both trials were similar, which suggested that the population in APL0406 may be similar to the population eligible for arsenic trioxide in England. The committee concluded that APL0406 was relevant to NHS clinical practice in England, and that AML17 was relevant as supporting evidence.

3 Committee discussion | Arsenic trioxide for treating acute promyelocytic leukaemia | Guidance | NICE Jun 2018

Importance of collaboration 1

Combining or meta-analyzing data

Trisenox

arsenic trioxide

On 13 October 2016, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending a change to the terms of the marketing authorisation for the medicinal product Trisenox. The marketing authorisation holder for this medicinal product is Teva B.V.

The CHMP adopted changes to the existing indication as follows[2]:

"Trisenox is indicated for induction of remission~~,~~ and consolidation in adult patients with ~~relapsed~~:

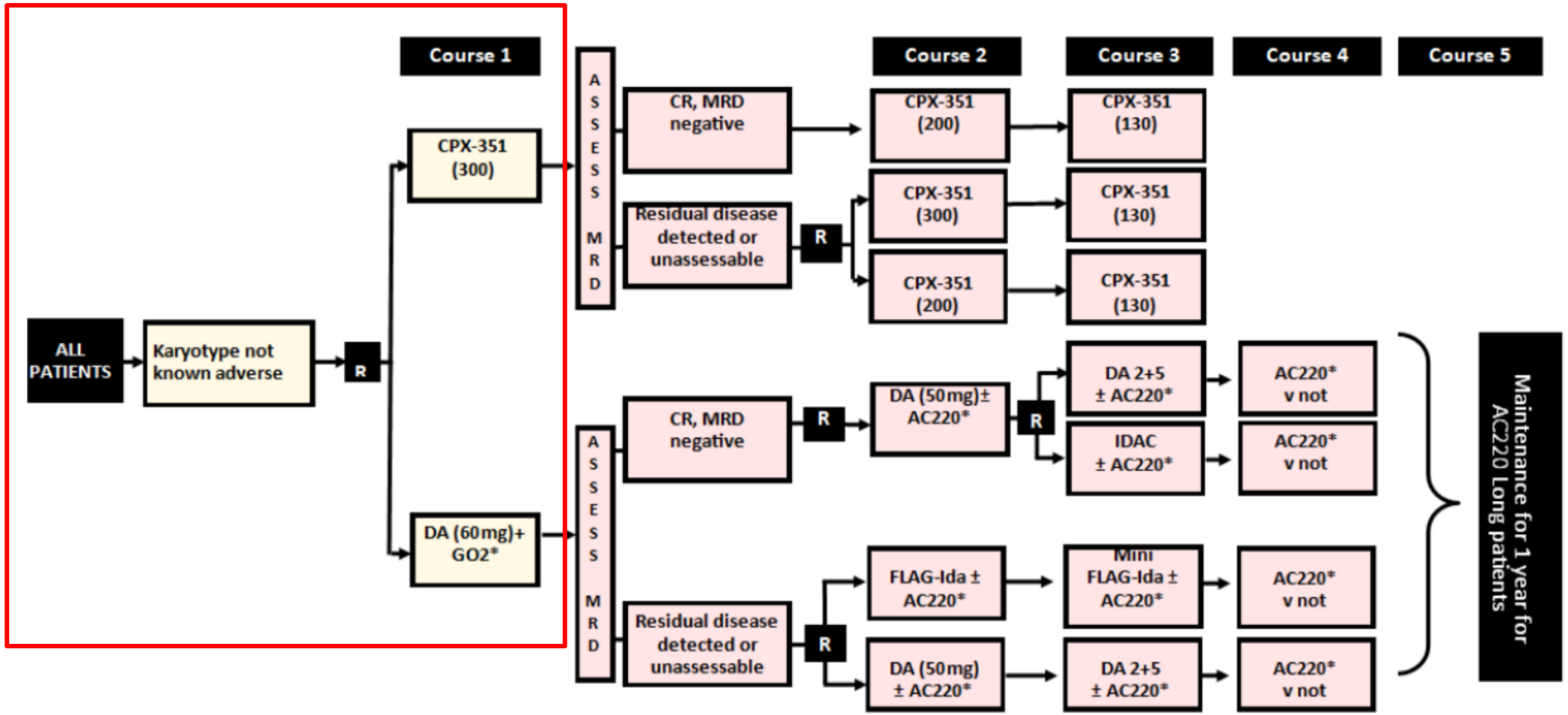
- **Newly diagnosed low-to-intermediate risk acute promyelocytic leukaemia (APL) (white blood cell count, ≤ 10 x 10^3/µl) in combination with all-*trans*-retinoic acid (ATRA)**
- **Relapsed/**refractory acute promyelocytic leukaemia (APL) **(previous treatment should have included a retinoid and chemotherapy)**

characterised by the presence of the t(15;17) translocation and/or the presence of the Pro-Myelocytic Leukaemia/Retinoic-Acid-Receptor-alpha (PML/RAR-alpha) gene. ~~Previous treatment should have included a retinoid and chemotherapy.~~

The response rate of other acute myelogenous leukaemia subtypes to ~~Trisenox~~ **arsenic trioxide** has not been examined."

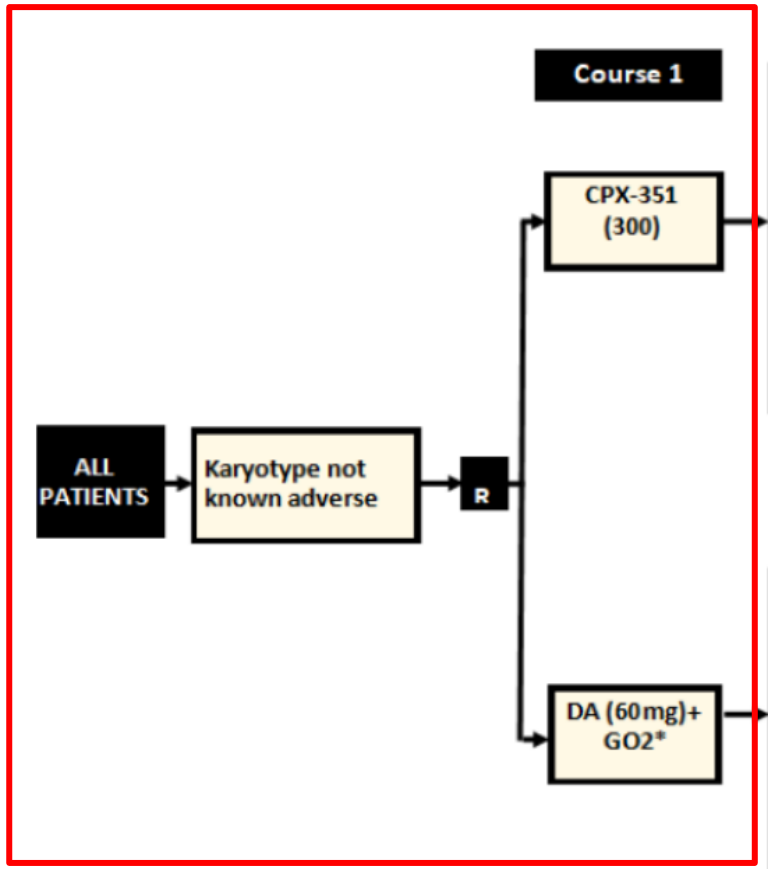
Detailed recommendations for the use of this product will be described in the updated summary of product characteristics (SmPC), which will be published in the revised European public assessment report (EPAR), and will be available in all official European Union languages after a decision on this change to the marketing authorisation has been granted by the European Commission.

Trisenox | European Medicines Agency (europa.eu) 2018

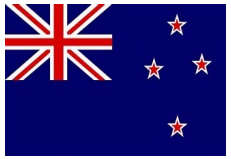


EORTC-QLQC30, EQ5D, HADS – baseline, 3 months, 6 months, 12 months

Importance of collaboration 2



Trial conduct



Induction CPX-351 v DA-GO2, DA only (UK)

Year *(add year)*	Projected number of patients recruited at the time of the application	Current revised projected number of patients recruited	Actual number of patients recruited
1 2019	20-25 patients per month		132
2 2020			85
3 2021		Revised 10-12 patients per month	107
4 2022			65
TOTAL			389

Induction CPX-351 v DA-GO2, DA only (international)

Year *(add year)*	Projected number of patients recruited at the time of the application	Current revised projected number of patients recruited	Actual number of patients recruited
1 2019	Detailed predictions by country were not provided		9
2 2020			30
3 2021			7
4 2022			16
TOTAL			62

AML18	Baseline	3 month	6 month	12 month
Overall	526 (86%)	369 (60%)	298 (49%)	222 (36%)
CR	306 (90%)	247 (72%)	207 (61%)	163 (48%)
No CR	220 (81%)	122 (45%)	91 (34%)	59 (22%)

Intensive treatment HR-MDS

LI1	Baseline	3 month	6 month	12 month
Overall	282 (94%)	157 (53%)	122 (41%)	74 (25%)
CR	81 (99%)	69 (84%)	66 (80%)	52 (63%)
No CR	201 (93%)	88 (41%)	56 (26%)	22 (10%)

Non-intensive treatment HR-MDS

AML18	Baseline	3 month	6 month	12 month
Overall	526 (86%)	369 (60%)	298 (49%)	222 (36%)
CR	306 (90%)	247 (72%)	207 (61%)	163 (48%)
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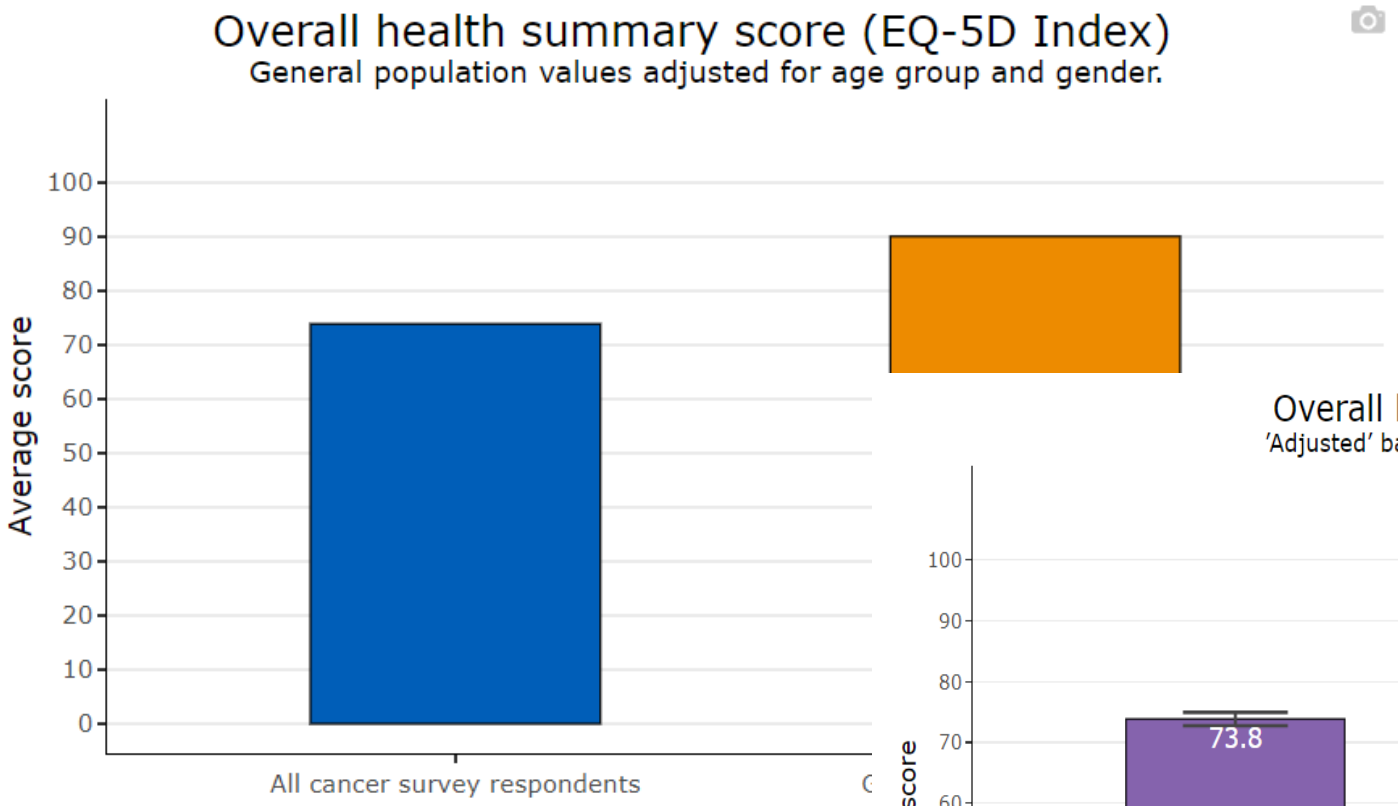
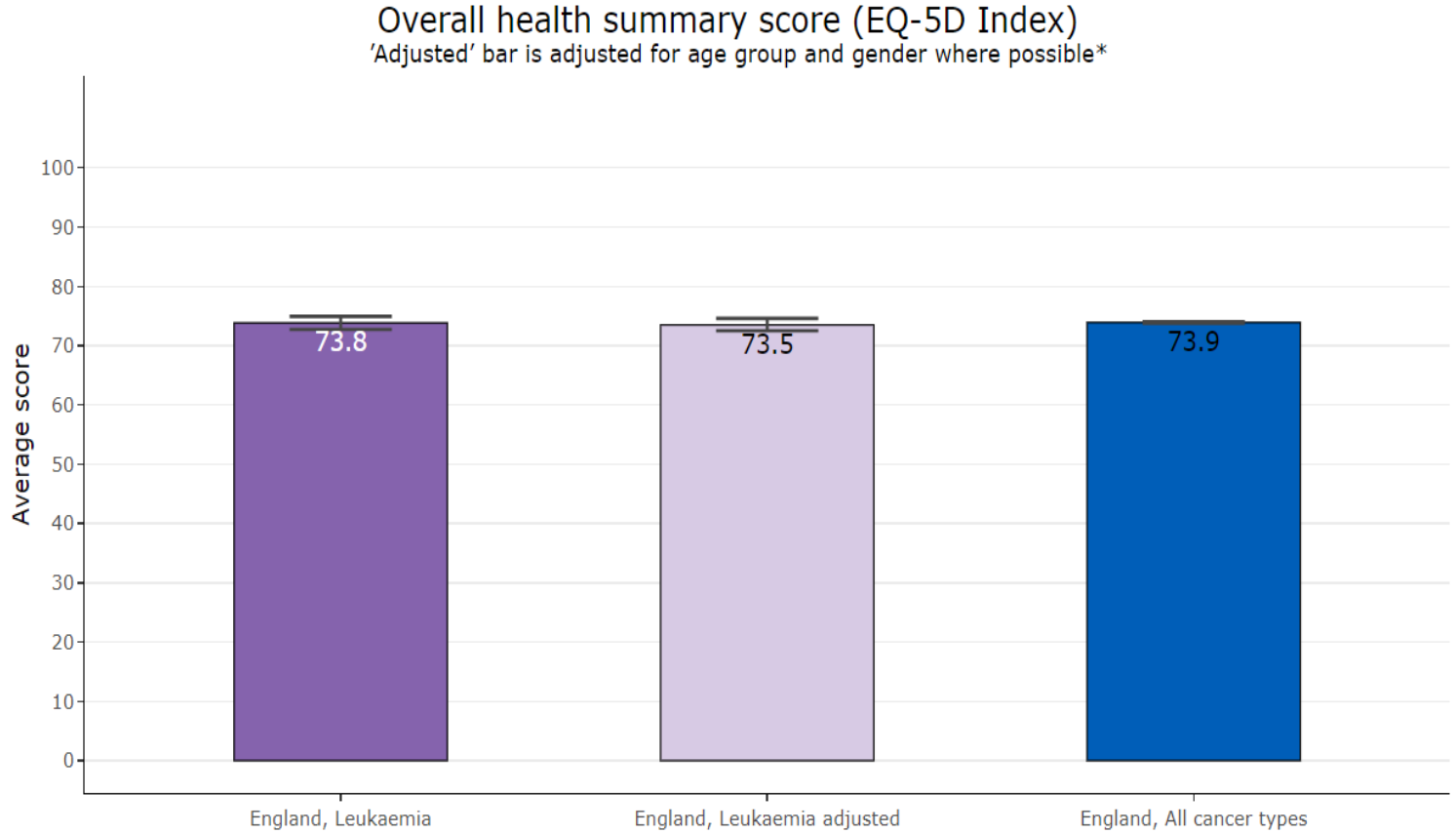
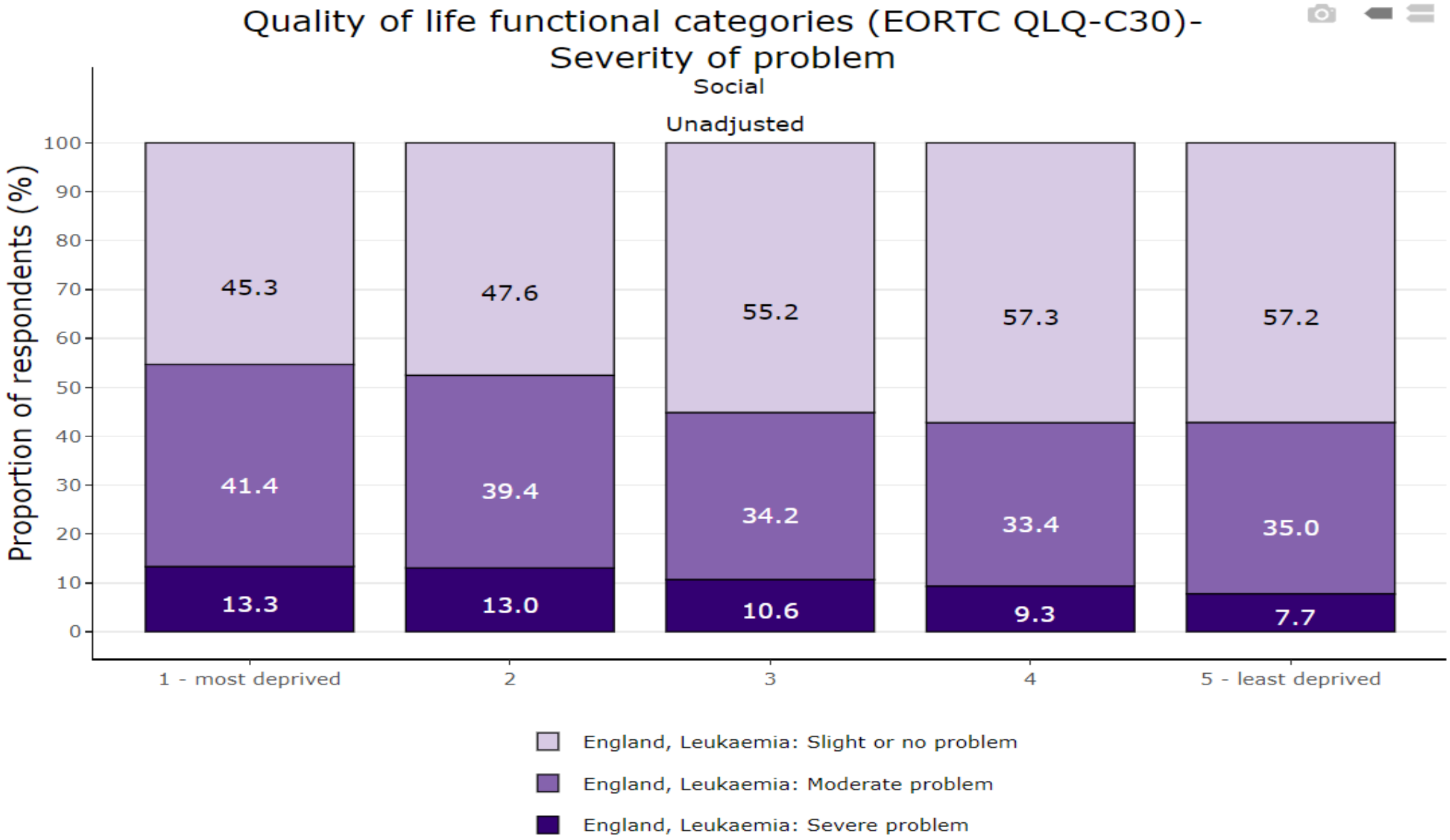
Non-intensive treatment HR-MDS

Data collection process

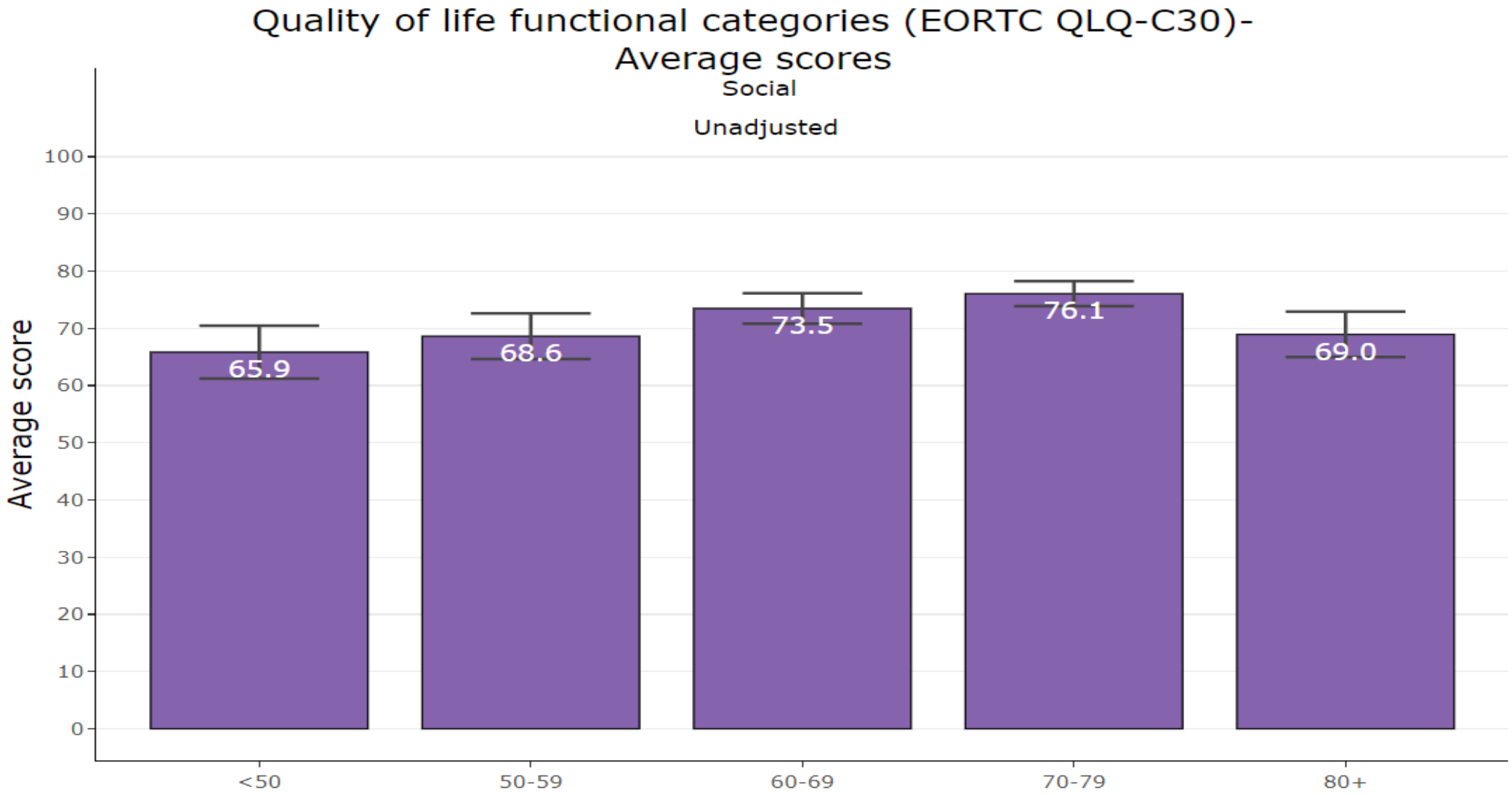


All cancer patients, approximately 18 months post-diagnosis

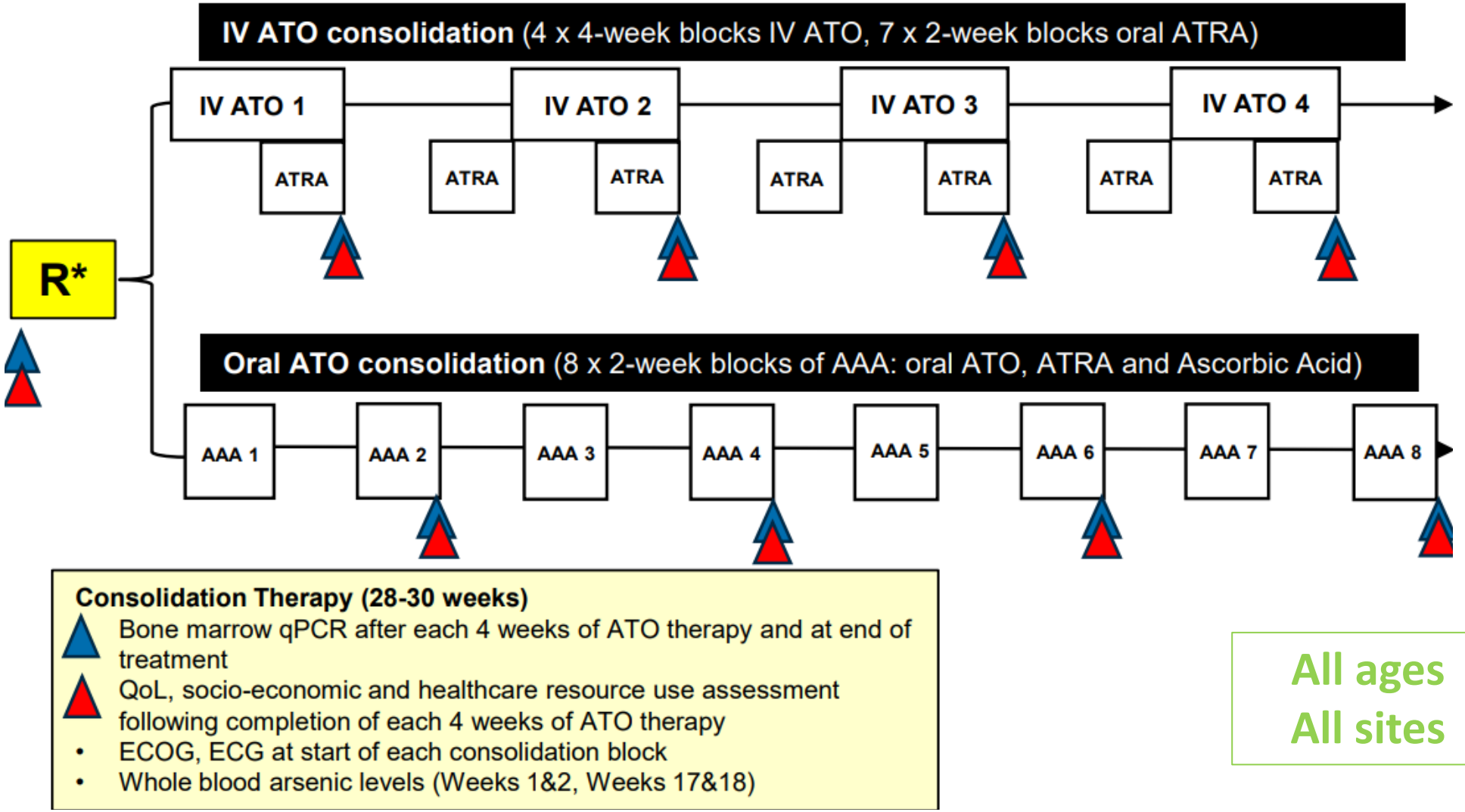



Quality of life functional categories (EORTC QLQ-C30)- Severity of problem
Social
Unadjusted
Proportion of respondents (%)
100
90
80
70
60
50
40
30
20
10
0
45.3
47.6
55.2
57.3
57.2
41.4
39.4
34.2
33.4
35.0
13.3
13.0
10.6
9.3
7.7
1 - most deprived
2
3
4
5 - least deprived
England, Leukaemia: Slight or no problem
England, Leukaemia: Moderate problem
England, Leukaemia: Severe problem

Importance of collaboration 3 Validate effects, inter-population



Working with GIMEMA



Consolidation Therapy (28-30 weeks)

- Bone marrow qPCR after each 4 weeks of ATO therapy and at end of treatment
- QoL, socio-economic and healthcare resource use assessment following completion of each 4 weeks of ATO therapy
- ECOG, ECG at start of each consolidation block
- Whole blood arsenic levels (Weeks 1&2, Weeks 17&18)

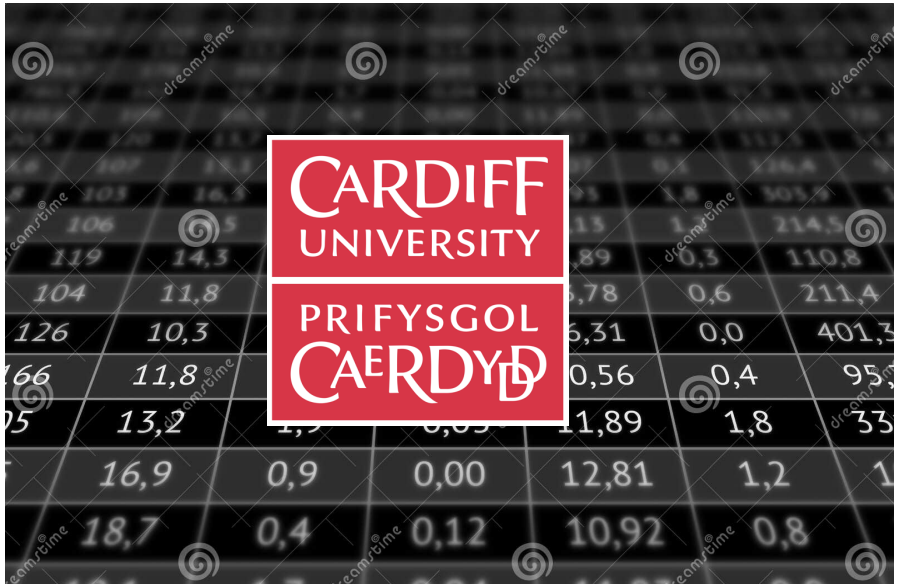
All ages
All sites

Working with GIMEMA

	APL	AML	MDS	TOTAL
Italy	520	1017	1146	2683
UK	206	816	810	1832
Canada	-	-	1500	1500
Total	726	1833	3456	**>6000 pts**

Create a **large international dataset** with clinical, survival and PRO information, which will allow us to answer several unique research clinical questions

Working with GIMEMA



Aims

- Embed QoL data collection into all future UK acute leukaemia trials
  - Aligned process, patient input
- Include rich demographic data
  - Ethnicity, socio-economics, distance travelled, etc.
- Build consensus between international groups about how to do this
- Make UK data available for future collaborations

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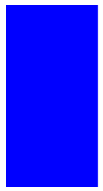
Questions?


HARMONY ALLIANCE