Quo vadis, Amyloidosis? Summary

We know where we have come from,

we are currently under way, and

we like to know where we are heading toward

Bouke P.C. Hazenberg, Groningen

Conflict of interests

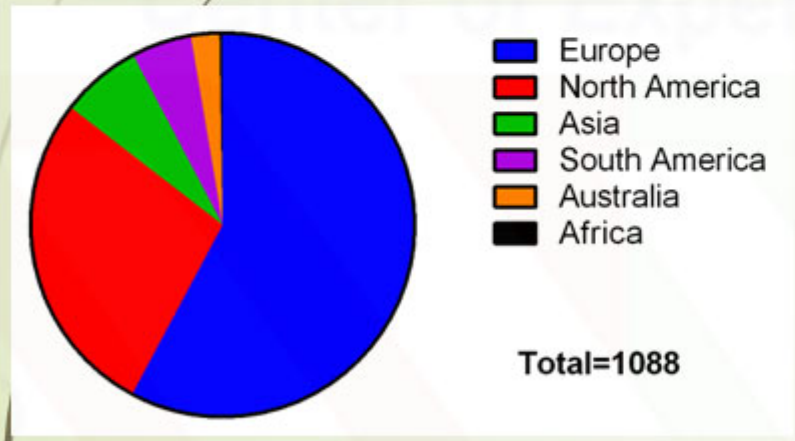
- No disclosures

18th International Symposium on Amyloidosis

- ISA 2022
- Symposium of 4 days in Heidelberg, minimal overlap of sessions
  - 25 lectures
  - 71 oral presentations
  - 309 poster presentations
  - 8 satellite symposia (25 % of the total time for lectures, orals, posters and satellites)
- Transparancy: 1.11 million euro sponsoring received from 19 sponsors
- Almost 1100 participants
  - 842 in person and 246 online
  - From 50 countries
  - A special welcome for the 3 participants of Africa!

ISA 2022:

1,088 participants of 50 countries



Europe	629
Germany	153
Spain	77
Italy	71
United Kingdom	52
France	42
Romania	29
Belgium	28
Switzerland	26
Sweden	24
Greece	21
Denmark	20
Portugal	19
Austria	18
Netherlands	17
Ireland	5
Norway	5
Russia	4
Bulgaria	3
Czech Republic	3
Slovakia	2
Slovenia	2
Cyprus	1
Finland	1
Guadeloupe (Fr)	1
Latvia	1
Martinique (Fr)	1
New Caledonia (Fr)	1
Poland	1
Ukraine	1

Australia	26
Australia	23
New Zealand	3

North America	301
United States	283
Canada	14
Mexico	3
Puerto Rico (US)	1

South America	55
Brazil	30
Argentina	19
Uruguay	3
Bolivia	1
Chile	1
Colombia	1

Asia	74
Japan	34
Israel	21
South Korea	6
India	5
China	2
Bangladesh	1
Hong Kong (C)	1
Jordan	1
Philippines	1
Singapore	1
Turkey	1

Africa	3
Algeria	1
Ghana	1
Morocco	1

Sunday 4

- Keynote lecture: aging of the immune system by Cornelia Weyand: many effects on T cells and on macrophages – we can learn how to look at aging
- Opening lectures:
  - AL amyloidosis model – leading the way to cure by Giampaolo Merlini: beautiful overview of AL amyloidosis and what it teaches us
  - Functional amyloid by Daniel Otzen: amyloid is regulated as an orderly process that is beneficial for the organism and not explosive because that is pathological
  - Gene targeting therapy in ATTRv amyloidosis by Julian Gillmore: complete precursor protein regression is beneficial in AA and AL, so regression should be >95%. Gene editing with NTLA (CRISPR-CAS9) may result in 93% regression and possibly even more
- Welcome reception: a warm and generous welcome for all of us!

Some basic research topics

- Genetics is underlying amyloidogenesis, clear risk factors for getting amyloid
- PTM: does N-glycosylation of the light chain play a role in amyloidogenicity?
- Mounting evidence for cardiotoxicity of light chains in AL
- Collagen associated with AL inhibits fibril phagocytosis
- Aggregation-prone regions (APR) are needed for fibril growth
- SerpinA1 has effects on the modulation of TTR proteolysis
- A long expected development is the new kappa knock-in + seeding mouse model of AL
- Also new are transgenic animal models of AL in C elegans and of ATTR in mouse

Monday 5

Merlini Award Ceremony

For Per Westermark, his lecture:

Amyloidosis: Reflections on passed and coming times

Some clinical research topics

- Artificial intelligence and machine learning emerge, e.g. in clinical detection of ATTRwt, in pathologic light chain detection, and in using ECG and imaging techniques
- Genes as risk factors for development, for prognosis (in AL), but also guide treatment
- Minimal/measurable residual disease (MRD) emerging concept in AL
- sST2 (soluble suppression of tumorigenesis-2) is a possible new serum biomarker in AL related to inflammation and fibrosis
- Neurofilament light chain is a serum biomarker of neuropathy
- Increased liver stiffness is a marker of liver amyloid
- Imaging of amyloidosis: role in recognition, disease severity, disease monitoring
- 124I-AT-01, a new promising tracer in amyloidosis

Tuesday 6

- Get together
- Challenging Cases
- Junior Meets Senior (Round Table)

New or potential treatment modalities

- **AL**: BCL-2 inhibitor venetoclax, belantamab mafodontin (anti-BCMA), BCMA-CART, CAEL-101, elotuzumab (binds SLAMF7), isatuximab (anti-CD38 mAb)
- **ATTR**: glavonoid (licorice-derived flavonoid oil) a natural tetramer stabilizer, eplontersen (anti-sense), acoramidis (AG10, stabilizer), NNC6019-0001 (antibody that binds all TTR except native TTR)
- **All amyloid**: Antibodies, e.g. birtamimab (NEOD001), AT-2 and AT-4 (pan amyloid binding fusion peptides), chimeric antigen receptor-macrophages (CAR-M) as a possible potential therapeutic for amyloid clearance
- **Supportive care**: Droxidopa (norepinephrine prodrug) for orthostatic hypotension, iv inotropic drugs, heart transplant in ATTRwt

Wednesday 7

- Conference Dinner and Award Ceremony

Final remarks

- Since the start in 1967, the focus of our symposia gradually moved from AA to AL and ATTR and from pathology to treatment modalities – few other types than AL and ATTR
- There is a steady growth in number of participants and countries of origin
- The online presence of posters increases their tenability and value!
- We all like to thank the pharmaceutical industry for their sponsoring of the symposium
- However, we clinicians and researchers should notice a consequence of our close and fruitful collaboration is a growing influence of pharma – stay independent!
- The symposium was very successful in the number, variety and quality of the presentations and the generous way we all were treated

We thank the organizers, especially Stefan and Ute, for this superb symposium!