Access to innovative cancer therapies: patients view

Pauline Evers – belangenbehartiger innovatieve therapie NFK

FIGON dagen 1-2 oktober 2018

Nederlandse Federatie van Kankerpatiënten organisaties

Presentation

1. Introduction NFK
2. ATMPs: where do we stand?
3. CART cells registered but still far from available for patients
4. Conclusion

nfk

NFK komt op
voor mensen met en na kanker.

19 verenigde kankerpatiëntenorganisaties

nfk

MISSIE

NFK komt op voor de belangen van kankerpatiënten en hun naasten. Tijdens én na hun behandeling, ongeacht de vorm van kanker. Wij geloven dat je mét patiënten moet beslissen, niet over patiënten. Daarom geeft NFK kankerpatiënten een duidelijke stem. In de politiek, in de media, in de zorg, in de wetenschap en bij verzekeraars.

VISIE

NFK is een slagvaardige onafhankelijke federatie. Wij werken samen met de kankerpatiëntenorganisaties op gedeelde thema's. De focus van NFK ligt op expertkennis, belangenbehartiging en ondersteuning van de kankerpatiëntenorganisaties.

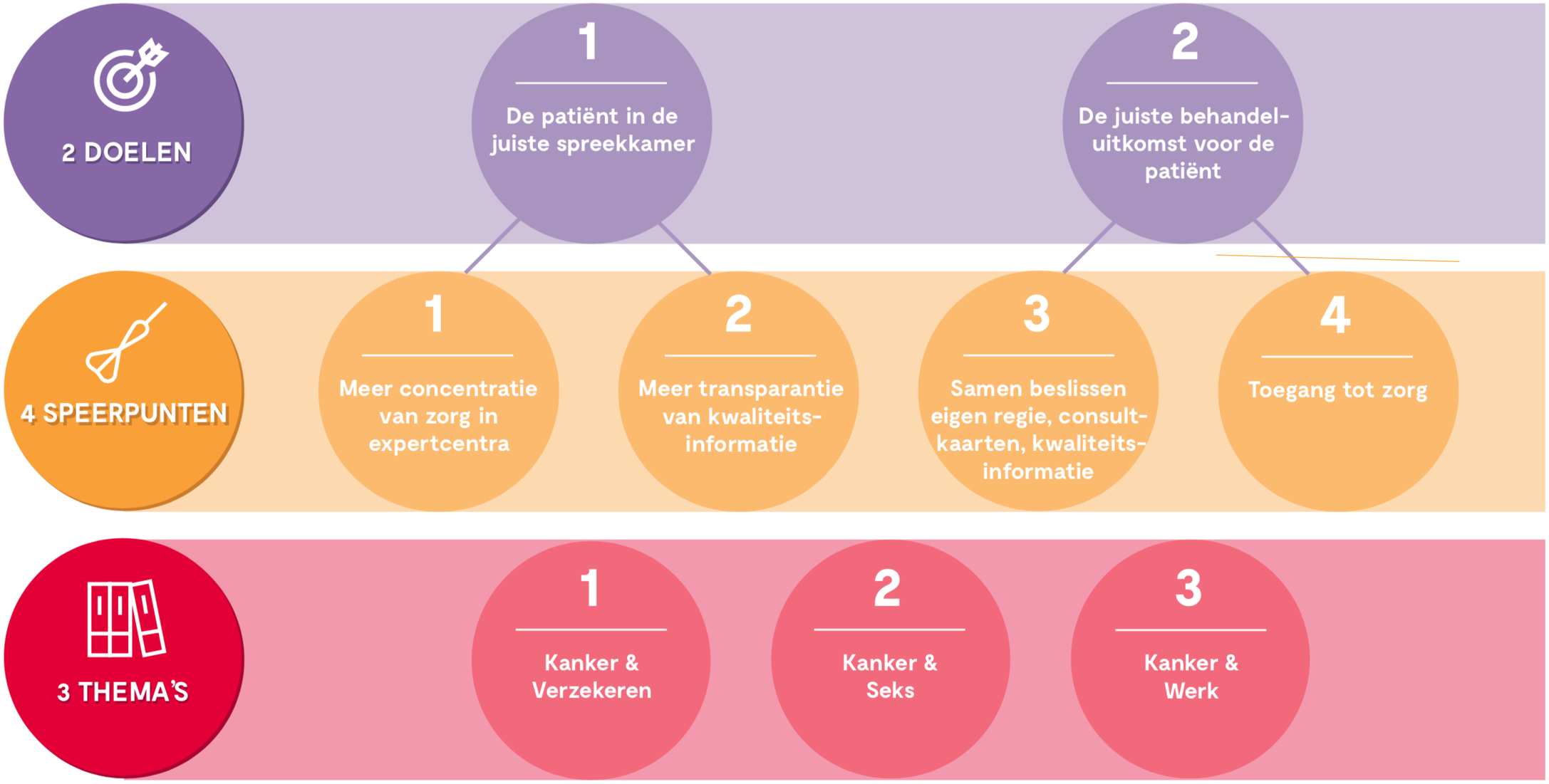
DOEL

Een betere kwaliteit van leven en een betere kwaliteit van zorg voor (ex-)kankerpatiënten en hun naasten.

STRATEGIE

Onze doelen bereiken we door de inzet van ervaringsdeskundige patiënten en professionele belangenbehartigers. NFK onderscheidt zich door actief naar de patiëntbehoeften te vragen via Doneerjeervaring.nl en daar de activiteiten op af te stemmen. NFK luistert naar en praat met álle stakeholders in het oncologisch veld. NFK wordt beschouwd als dé stem van de patiënt.

nfk


2 DOELEN
1
De patiënt in de juiste spreekkamer
2
De juiste behandel-uitkomst voor de patiënt
4 SPEERPUNTEN
1
Meer concentratie van zorg in expertcentra
2
Meer transparantie van kwaliteits-informatie
3
Samen beslissen eigen regie, consult-kaarten, kwaliteits-informatie
4
Toegang tot zorg
3 THEMA'S
1
Kanker & Verzekeren
2
Kanker & Seks
3
Kanker & Werk

Input from patients through patient organisations is important

- Patients have experience with their disease and they have a holistic view
- Based upon input of member organisations and individual experience of patients
- Based upon our survey tool, ‘doneer je ervaring’ (cancer patients at large)

Input communicated to other stakeholders

- By NFK and member organisations advocates
- By individual patients of our organisations (guideline develoment, input in scientific research, audits in hospitals)
- Focus groups, surveys
- Direct interactions of patients with health care workers (Els Borst talks, visits to hospitals)
- Publications (scientific and press), presentations on symposia

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ATMPs where do we stand?

ATMPs in Europe (2009- 2017)

EUROPEAN MEDICINES AGENCY

~ 500 clinical trials using ATMPs in EU

~ 290 ATMP classifications

~ 270 scientific advice requests

19 MAAs reviewed

10 ATMPs approved

3 withdrawn
1 Suspended

Market

6
licensed
ATMPs

2nd International Awareness Session - The EU medicines regulatory system and the European Medicines Agency Presented by Patrick Celis on 8 March 2018 CAT Secretariat

ATMPS where do we stand?

EUROPEAN MEDICINES AGENCY

Conclusions

- ATMP Regulation provides a clear regulatory framework for ATMP developers
- The approval of products for each of the 3 categories (GTMP, CTMP, TEP) indicates that the system is workable
- Incentives (ATMP specific, other)
- Most activities of the CAT in the pre-submission phase (SA, classification)
- Lot of ATMP clinical trials (review and approval of CTs by national authorities)
- ATMP developers need support from authorised (before, during and after MAA)

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EMA registered

13 ATMPs authorised, 9 still on the market (3 Gene therapy, 5 Cell therapy, 4 Tissue)

Holoclar – Tissue, to treat (chemical) burns in the eye 2015
Imlygic – Gene therapy, melanoma 2015
Strimvelis – Gene therapy, ADA-SCID 2016
Zalmoxis – Cell therapy, as adjunct in Stem Cell Transplantation to prevent GvHD while maintaining graft vs leukemia effect 2016
Chondrosphere – Tissue, to treat knee cartilage defects 2017
Alofisel – Cell therapy, to treat fistula in Crohn's disease 2018
Yescarta CART hematological malignancy 2018
Kymriah CART hematological malignancy 2018
Luxturna Gene therapy, inheritable eye disorder 2018

4 are withdrawn for commercial reasons(Chondrocelect (tissue, to treat knee cartilage defects), Glybera (Gene therapy for metabolic disease), MACI (tissue to treat knee cartilage defects), Provenge (Cell therapy, prostate cancer)

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Problems encountered

Presentations of today show lot of issues in development

- Sometimes science
- Sometimes technical (production issues, GMP)
- Sometimes clinical (get the product in the right target organ, side effects)
- Lack of knowledge of regulatory requirements

Availability after market authorisation?

- HTA REQUIREMENTS
- Pricing
- Additional technical licenses
- Practical implementation issues (logistics, identifying right patient group, product available, adverse event management)

Presentation

1. **Introduction NFK**
2. **ATMPs where do we stand?**
3. **CART cells registered but still far from available for patients**
   (around 20 ALL and 125 DBLBCL per year)
4. **Conclusion**

CAR T-cells Main clinical benefit – ALL

Kymriah

Table 2. Efficacy of available treatments for paediatric and young adult r/r ALL patients

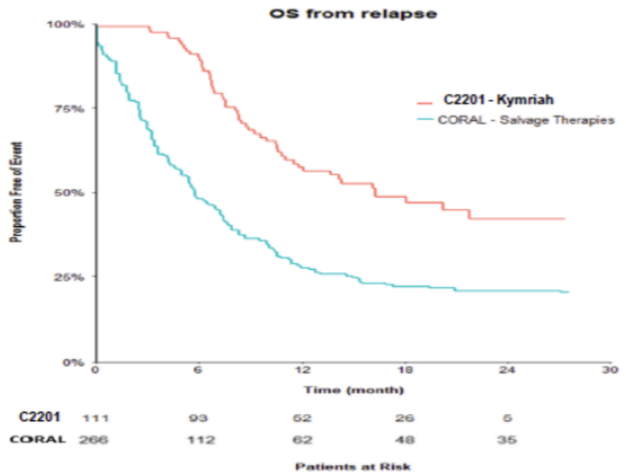
	Clofarabine mono[1]	Clofarabine+ etoposide+ cyclo[2]	Clofarabine+ etoposide+ cyclo[3]	Blinatumomab[4]	CTL019 B2202[5]
Patients, N	61	25	17	70	75
≥3 prior regimens	62%	28%	NA	7%	60%
ORR (CR+CRi)	20%	44%	76%	39%	81.3%
Median OS	**3.0 months**	**2.5 months**	**9.0 months**	**7.5 months**	**19.1 months**
12 months OS	20%	30%	33%	40%	76.4%
Early mortality (within 30 days)	25%	20%	NA	7%	3%

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Assessment_report_on_maintenance_of_orphan_designation/human/004090/WC500255533.pdf

CAR T-cells Main clinical benefit – DLBCL

Kymriah

Figure 2.



CORAL curve was truncated at the maximum follow-up for C2201

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Assessment_report_on_maintenance_of_orphan_designation/human/004090/WC500255533.pdf

Yescarta

Table 2. Response rates and OS in Patients with DLBCL in ZUMA-1 (pivotal) and SCHOLAR-1 (control).

	ZUMA-1 (N= 93)	**SCHOLAR-1 (N=462)**
ORR (%) [95% CI]	84 (75, 91)	26 (22, 30)
CR (%)	57	9
Duration of Responsea, median (months) [95% CI]	8.1 (2.4, NR)	NA
Duration of Responsea, CR, median (months) [95% CI]	NR (11.1, NR)	NA
Overall Survival, median (months) [95% CI]	NR (11.5, NR)	6.6 (6.1, 7.6)
6 month OS (%) [95% CI]	79 (69, 86)	56 (51, 60)
12 month OS (%) [95% CI]	59 (49, 68)	28 (24, 32)
18 month OS (%) [95% CI]	50 (37, 61)	24 (20, 28)

[a] Minimum follow-up of 12 months with median follow up of 15.1 months.

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Assessment_report_on_maintenance_of_orphan_designation/human/004480/WC500254963.pdf

Post marketing issues The Netherlands - Health technology assessment and price negotiations

- In general medicinal products in hospital are automatically reimbursed as of the moment of marketing authorisation
- Small number in the ‘sluis’ (lock) for price negotiations based on health technology assements through Zorginstituut Nederland

For CART cells

- Products are quite expensive –VWS decided to put them in de SLUIS (lock)
- ZINL is going to assess based on dossier supplied by industry. Criteria: therapeutic added value, cost effectiveness and budget impact. Timeframe 4 months
- VWS will start price negotiations: anything between 3 and 10 months

Risk minimisation plan and training in hospitals- Clinic

CAR Tcells have serious side effects

1. Cytokine release syndrome, ≥grade 3 in 13% of patients. To be treated with tocilizumab
2. Neurological toxicities, ≥grade 3 in 31% of patients

- All hospitals and hospital personal needs to be trained and certified by the companies to fullfill special criteria as specified in the risk evaluation and managent plan. EU requirement. Training and certification through the manufacturing companies.
- Special educational material to be developped for patients regarding adverse events and safety: companies together with CBG (EU requirement)
- Patients need to stay in proximity of treating hospital for 4 weeks after infusion to be able to react quickly in case of serious adverse events

Additional Dutch licences, procedures can only start after Marketing authorisation - ATMP related

GMP certificates through Inspection ‘Gezondheidszorg en Jeugd’

- Per hospital but also for the Dutch affiliates of the manufacturing companies although cell samples will not be physically transported to their premises but shipped directly from hospitals to plants abroad

GMO license through Ministry of ‘Infrastructuur en Waterstaat’

- Per hospital but also for the Dutch affiliates of the manufacturing companies although cell samples will not be physically transported to their premises but shipped directly from hospitals to plants abroad, https://loketgentherapie.nl/??

Acknowledgement of the facility to allow storage of tissues and organs, (WVKL erkenning, wet veiligheid en kwaliteit lichaamsmateriaal) to be obtained through an application at Farmatec. (https://www.farmatec.nl/vergunningen/erkenning-weefselinstelling---orgaanbank), procedure takes 120 days

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CONCLUSION

- Patients are hoping for new therapies
- Unrealistic hope sometimes comes from over-enthusiastic researchers and even more from the media
- So, be realistic and careful with all communication in the press, to patients and to the general public
- When starting development, keep the end in mind, not the short term:
  be aware of all requirements pre- and post marketing (more suggestions to follow in next talk)

WHEN LIFE OF PATIENTS IS AT STAKE

PATIENTS DO HAVE NO TIME TO LOOSE

WE DO WANT TO HAVE QUICK ACCESS

BUT ONLY TO EFFECTIVE AND SAFE PRODUCTS