# Opportunities and Threats

## Economics and Access, Health Care Systems and Novel Therapies

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# Haemophilia – Current Standard of Care

- Clotting Factor Concentrate (CFC) based
- Comprehensive Care Centre (CCC) coordinated

- Severe forms – self-sufficiency (prophylaxis)
  - EHC advocacy - Minimum units/capita/country

- Non-severe forms – hospital dependent (on demand)

- Chronic inhibitor patients – medically disadvantaged - less efficacious therapeutics

# Current Landscape

- Cost lies predominantly with prophylaxis
  - Prophylaxis results in a bleed free subgroup, but **not** majority
- Number of “Severe” PWH – surrogate metric of judging a clinic’s expertise.
- Bleed and treatment burden and pathways for treatment access for “non-severe” PWH  less well understood
- Trough thresholds for prophlaxis protection are increasing
  - Clinical data, EHL, novel agent and gene therapy expectations

# Novel agents

- Biphenotypic antibody (Emicizumab)
- Interfering RNA  (Fitusiran)
- Anti-TFPI strategies
- Gene therapy/editing strategies

# “Promise” of novel agents’ (including gene therapy)?

- In contrast to peaks and troughs of current CFC use , to establish a new and constant baseline  of protection well above conventional trough baselines of current standard of care (1-5iu/dl)

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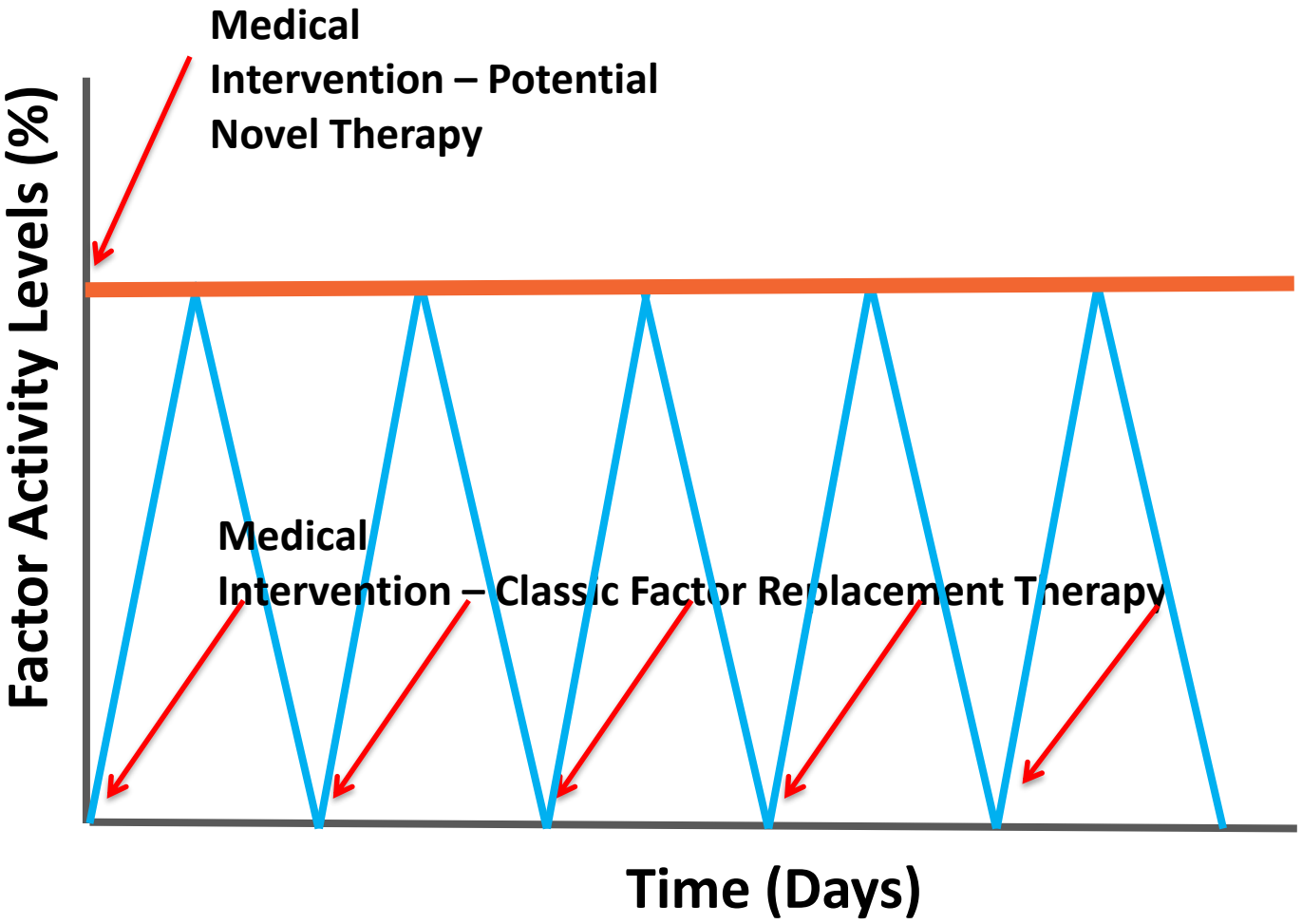

# “Promise” of novel agents’ (including gene therapy)?

- In contrast to peaks and troughs of current CFC use , to establish a new and constant baseline  of protection well above conventional trough baselines of current standard of care (1-5iu/dl)

- Likely >10iu/dl factor equivalent
- Possibly >20 iu/dl factor equivalent
- May achieve >50iu/dl factor equivalent

# Current changing landscape

- Increasing Commercial Competition
  - Between CFC companies
  - CFC companies against novel therapy companies

- Price reduction – particularly CFC
- Tender processes harnessing this
  - eg PARTNERS, UKHCDO
- Exaggerating price differences across Europe
  - Between countries
  - Between products
  - Challenge for pharma colleagues to enter markets

# Opportunities for conventional CFC treatment strategies

- Increasing affordability
- Increasing availability
- Increasing access
- Increasing personalisation (eg PK tailoring)
- Increasing trough expectation (both SHL &EHL)
- Increasing protection
- Increasing participation in registries
  - National and European

# Threats to conventional CFC treatment strategies

- **Missing all previous opportunities due to distraction by novel agent "promise".**
- Educational need to maximise the CFC opportunities
  - Eg pharamcokinetic tools, Lab assay needs & differences
- Increasing number of marketed molecules
  - both SHL & EHL –
    - mechanistic and educational nuances differ for each
  - Decreased power to detect adverse events
  - Need for active not passive surveillance

# Novel Technologies

- **Prophylaxis not bleed treatment therapeutics**

- Appear to demonstrate superiority over bypass agents in prophylaxis for inhibitors.
  - Paradigm change for chronic inhibitor patients

- **Opportunity** – may demonstrate superiority over CFC prophylaxis in non-inhibitor patients?

- **Threat** - miss opportunity to demonstrate/quantify superiority
  - ***no Randomised Controlled Trial (RCT) planned yet to interrogate this hypothesis***
  - RCTs needed to leverage health care policy change
  - Absence of RCT evidence may delay, limit future access

# Depersonalisation of care with novel agents?

- **Opportunity**
  - One dose-size fits all – no tailoring
  - Infrequent, easy dosing (sub cut, SC not IV)
  - All treated become safely “mild” phenotypes

- **Threats**
  - Distracted from optimising CFC access and treatment strategies
  - Managing changing expectations
    - Patients, families, treaters, commissioners etc
  - Implementation brings dramatic treatment paradigm shift
    - Challenging established patient and treaters knowledge and treatment algorithms

# Inhibitor Setting and Novel agent

- **Bleed treatment Paradigm shift – happening now**
  - Treat ***as soon as possible*** vs ***Watch & Wait***
  - Concern about serious adverse events on trial
    - Including thrombotic microangiopathies and death
    - Possibility of undertreating bleeds trying to minimise SAE risk
- **Opportunity**
  - Shared, real-world experiential learning
  - New guidelines – eg imminent UKHCDO guidelines
- **Threat**
  - Rushed implementation, outside Comprehensive care
  - Poor communication, poor bleed treatment planning
  - Further, but avoidable serious adverse events, inc.deaths
    - Risk to clinicians overseeing care
    - Risk to PWH and families

# Adverse Events

- Known unknowns
- Unknown unkowns

- **Opportunity**
  - Consolidating contributions to national and european registries
- **Threat**
  - Not prioritising and re-focusing surveillance
  - Missing short, medium and long term signals of adverse events (over months, years and decades)

# Does comprehensive care have a future?

- Arguably, if all severes' phenotypes changed to mild – current metric implies substantially reduced burden on CCCs.

- Contrary position – they all are better managed , less frequent bleed/trauma/procedure events
- **BUT….**
- Increased dependency and risk when (not if) events occur
  - Need clear Emergency pathway of access
  - dependency on hospitals for IV CFC replacement
  - Continued and changing educational/advocacy needs

# Novel Technologies - implementation

- **Need & Opportunity**
  - Education, education, education
  - Empower care staff, PWHs and families
  - Partnerships with Pharma to prioritise CCC access
  - European Reference Network value
- **Threat**
  - Undermining of comprehensive care structure
  - Dissolution of coordinated post marketing surveillance and advocacy potential
  - Missed opportunity to maximise CFC strategies

# Vision

- Likely co-existence of multiple modalities of treatment for haemophilia A&B

- Patient centric care and choice
  - Needs appropriate patient education
  - Needs appropriate clinician education
  - Needs appropriate evidence base
  - Needs appropriate studies (eg RCT) and registry data

# Vision

- Comprehensive care will continue to be pivotal to future generations of persons and families with haemophilia

- Transparent/equitable choice and access to most efficacious and safe treatment for that individual living with haemophilia at that time of their life.