Early access to medicinal products

potential and limits

European Genetic Alliances Network

www.egan.eu

Dutch Federation of Cancerpatient organisations

www.nfk.nl

ECRD Berlin

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Asked by the organisation to make some critical remarks

Therefore, statements in this talk do not necessarily reflect the opinion of the organisations I am representing

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Current ‘early access’ procedures (1)

- Conditional approval (15 products so far)
  - Lifethreatening disease, orphan drugs, emergency situations
  - the risk-benefit balance is positive;
  - applicant is able to provide the comprehensive clinical data at later stage;
  - the benefit of immediate availability outweighs the risk inherent in the fact that additional data are still required
  - Re-assessment on yearly basis

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Current ‘early access’ procedures (2)

- Registration under exceptional circumstances (28 so far) for which data cannot be supplied because
  - Indications is very rare
  - Scientific knowledge is insufficient
  - Collecting data is considered unethical
- obligations
  - Reviewed annually to re-address risk / benefit
  - Submit data, limitation to prescription

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Early access (3)

- Compassionate use in various countries, national legislation
- CHMP can give advice upon request of natl competent authorities: untill now 4 products (2 hep C treatments, antiviral, …..)

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Adaptive licensing

- Staggered approach
- Registration based on phase 2 …..
  - Unmet need
  - Very promising efficacy data, possibly on surrogate markers
  - Sufficient trust in safety
- With a commitment for further research after registration:
  - Strict follow up of all pats treated in the (limited) registered indication (registers on EU level)
  - Clinical studies to broaden the indication

  - EMA/254350/2012 Pilot on adaptive licensing

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Current procedure-example 1

- Product in melanoma
  - severe form of melanoma, RR 15%, OS very limited, mainly younger patients (30-40 yrs), no Rx available
  - Phase 2 data indicate promising results, most responders (around 20% of patients treated) survived significantly longer
  - Could have been a reason for adaptive licensing
  - In phase 3 response duration has been confirmed in RCT.
  - After MA further survival analysis points into the direction of even longer OS and may be definitive cures.

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Adaptive licensing- example 1

- RCT is needed to confirm efficacy for full license – possibilities to execute such trial is difficult after adaptive licensing
- During phase 3 and registration phase patients were dying who could have been saved in case of early access
- With adaptive licensing ALL patients could have had earlier access

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Current procedure-example 2

- Product in Duchenne
  - Phase II data were very promising showing significant improvement of primary endpoint (6MWT)
  - Phase III trial failed primary endpoint (6MWT) as well as most secondary endpoints
  - Program is on hold now

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Adaptive licensing- example 2

- In case of adaptive licensing many more patients might have had access to the product
- What are the possibilities to withdraw the license when responding patients are on treatment?
- Due to detailed data collection in phase 3 trial it might be possible to identify subpopulation for response

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pros

- Early access for patients in limited indication
- Possibility to start collection of data in daily practice at an earlier stage
- More centres can gain experience with the product at an earlier stage

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Issues to solve

- What if a product fails at later stage?
- At start only available for limited pat population?

- Reimbursement agencies might not be willing to reimburse
- Industry should be prepared to start with lower prices
- Difficulty in collecting post marketing data sufficiently robust for further licensing?
- Ethical to conduct further randomised trials?
- Possibility for creating unequal access between member states
- Early access vs orphan designation

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Way forward for adaptive licensing?

- Pilots under consideration
- Careful selection of eligible products
- Reimbursement agencies need to be on board
- Look into product's lifelong data collection (possibility for further RCT, data collection in registries)
- What to do when product fails: exit strategy

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In parallel initiatives

- Start registries as early as possible
- Disease orientated, not product orientated
- Joint scientific advice regulatory and reimbursement agencies
- Discuss patient relevant outcomes
- Increase use of conditional approval and exceptional circumstances

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questions

What are the opinions from the audience on the way forward