Perspectives from the rare cancer community

The Research Community’s Perspective

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EORTC
AGENDA

• Impact on conducting clinical research during the pandemic
• Impact on researchers
• Lasting changes for clinical research
Impact on Conducting Clinical Research during the Pandemic
Impact on Research Projects

Data integrity

↑

Operational Burden

↑

Research Project

Enrollment

↓

Safety of pats in ongoing trials


• Compliance with the GCP
• Deviations to protocol-requirements and procedures

↑↑ Study duration & costs
Impact on Enrollment
Clinical Research-Impact on enrollment

- Drop in cancer diagnosis
- Reorganization of health services
- Change in trial programs
- Consent process
- ↓ Screening activities

Enrollment paused
In Spain* with the comparison of new diagnoses in 2019 and 2020 over 400,000 patients:

- The observed ratio of new diagnoses between 2019 and 2020 was an average **decline of 31.1%** in new diagnoses. **Cancers** experience the largest **decline (49.7%)**.

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Decline (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>17.9</td>
</tr>
<tr>
<td>Bowel</td>
<td>31.7</td>
</tr>
<tr>
<td>Sarcomas and mesotheliomas</td>
<td>50.2</td>
</tr>
</tbody>
</table>

In The Netherlands**

- The Cancer Registry has seen a **40% decline** in weekly cancer incidence,

In the United Kingdom**

- UK has experienced a **75% decline** in referrals for suspected cancer


Period from May to October 2020 → prioritizing COVID-19 research & redeploying research staff

On 16th March 2020 a directive ordered:

- The suspension of all non-COVID-19-related research
  - EXCEPT the studies where research was the standard of care, for example, with experimental cancer treatments.
- The reorientation of research capacity towards the effort to develop COVID-19 treatments and vaccines

### Redeployment to Front line care

- 165 clinical research staff reduced by 79% → 131

### Redeployment to non clinical roles

- 52 non clinical research staff

<table>
<thead>
<tr>
<th>Clinical research staff redeployed to clinical roles</th>
<th>Destination</th>
<th>No.</th>
<th>Non-clinical research staff redeployed to non-clinical roles</th>
<th>Role</th>
<th>Destination</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Research Nurse</td>
<td>ICU, COVID wards, NHS Nightingale London Hospital</td>
<td>50</td>
<td>Non-clinical R&amp;D Staff</td>
<td>Ward clerks</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Paediatric Research Nurse</td>
<td>Evelina clinical activity, NHS Nightingale London Hospital</td>
<td>27</td>
<td>Project Managers</td>
<td>Tactical sub-groups</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Research Midwife</td>
<td>Routine clinics, maternity helpline</td>
<td>24</td>
<td>Research Technicians</td>
<td>Viapath</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Clinical Research Practitioner</td>
<td>ICU turning team</td>
<td>14</td>
<td>Research staff</td>
<td>Data entry</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Unassigned</td>
<td></td>
<td>16</td>
<td>Research staff</td>
<td>Bereavement centre</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Research staff</td>
<td>Cancer centre outpatient clinics</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td>131</td>
<td><strong>TOTAL</strong></td>
<td></td>
<td>52</td>
<td></td>
</tr>
</tbody>
</table>

Reference: National Institute for Health Research. DHSC issues guidance on the impact of COVID-19 on research funded or supported by NIHR 2020 [01/05/2020]
Change in Trial Programs

To provide access to experimental treatment potentially beneficial to patients but keeping them safe, Academia modified their clinical trial programs:

» Centers kept continuing trials for up to 20% of participants, based on participants’ needs, safety, and disease severity. In this case, measures were taken to minimize exposure to the staff and participants.

» Centers stratified trials based on their chance of success with interruption of those in absence of clear benefit.

» Centers continued ongoing trials but limited the activation of new ones.

Decisions from Pharmaceutical companies

» Lilly delayed the start of most new trials and paused enrollment in most ongoing trials

» Pfizer released a similar plan.

» Bristol-Myers Squibb did continue enrollment in existing trials but postponed activation of new trial sites and new trials

Consent Process

Ethical Standard

To protect patients

Face to Face meeting

To explain the study & expected benefits/risks

Alternatives

• Telephone
• Video-conference
Screening Activities

- Reorganisation of health care resources
  - Redeployment and repurposing (staff, activities related to clinical research) → affect capacity
  - Increased workload for medical and research staff
- Change in clinical trial programs
- Suspension of medical/surgical procedures
  - Impact on screening activities (imaging procedures, biopsies…)
  - Impact on collection of biomaterial (tumor tissue, blood samples) → impact of biomedical research
- Exposure risk to consider before participating
Benefits

- Opportunity of new treatment
- Oversight of patients in trials

Risks

- Patient (comorbidities, long distance travel, access local health service)
- Experimental treatment (side effects, access)
- Risk of acquired infection
- Conditions for safety monitoring

Participant
Implementation of preventive measures (lock downs, social distancing, limited access to beds)

Change of practice by investigators:

- Interruption or delayed screening activities & enrollment: 60% investigators
- Reprioritization enrollment → higher-priority trials: 50% investigators
- Permanent interruption: 20% investigators
- ↓ Rate of enrollment: 60% investigators


# Impact on Enrollment

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>All countries, All Therapeutic areas</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All countries, All Therapeutic areas</td>
<td>-65%</td>
<td>-79%</td>
<td>-74%</td>
</tr>
<tr>
<td><strong>Asia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>-68%</td>
<td>-33%</td>
<td>-49%</td>
</tr>
<tr>
<td>India</td>
<td>-84%</td>
<td>-97%</td>
<td>-95%</td>
</tr>
<tr>
<td>Japan</td>
<td>-44%</td>
<td>-69%</td>
<td>-72%</td>
</tr>
<tr>
<td>South Korea</td>
<td>-61%</td>
<td>-42%</td>
<td>-54%</td>
</tr>
<tr>
<td><strong>Europe</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>-68%</td>
<td>-81%</td>
<td>-76%</td>
</tr>
<tr>
<td>Germany</td>
<td>-33%</td>
<td>-77%</td>
<td>-81%</td>
</tr>
<tr>
<td>Italy</td>
<td>-53%</td>
<td>-49%</td>
<td>-65%</td>
</tr>
<tr>
<td>Spain</td>
<td>-68%</td>
<td>-82%</td>
<td>-68%</td>
</tr>
<tr>
<td>United States</td>
<td>-66%</td>
<td>-83%</td>
<td>-73%</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>-80%</td>
<td>-95%</td>
<td>-100%</td>
</tr>
<tr>
<td><strong>Therapeutic areas</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>-69%</td>
<td>-95%</td>
<td>-91%</td>
</tr>
<tr>
<td>CNS**</td>
<td>-68%</td>
<td>-76%</td>
<td>-75%</td>
</tr>
<tr>
<td>Endocrine</td>
<td>-64%</td>
<td>-91%</td>
<td>-89%</td>
</tr>
<tr>
<td>ID/ Anti infectives</td>
<td>-47%</td>
<td>-66%</td>
<td>-52%</td>
</tr>
<tr>
<td>Oncology</td>
<td>-48%</td>
<td>-60%</td>
<td>-58%</td>
</tr>
<tr>
<td>Respiratory</td>
<td>-34%</td>
<td>-86%</td>
<td>-81%</td>
</tr>
</tbody>
</table>

* YoYD = year-on-year difference; ** CNS = central nervous system

**References:**
Clinical Research-Challenges for the Ongoing Trials

Pandemic markedly affected the ability to conduct trials in safe and effective ways:

» Participant ability or willingness to come to hospitals

» Disruption to supply chains (drug, equipment) due to closed borders

» Limited resources (reorganization/redeployment) and time spent to implement alternatives for participants

» Significant disruption to study protocols
  • Major impact: social distancing impacting tests, investigations, in-person visits.

» Forced adaptation of research protocol (consent process remotely, telemedicine, treatment at home) with emergency amendments

» Treatment delayed or omitted doses
  • Participant with long distance travel (↑risk of acquired infection, national limitations to travel, quarantine)

» Change in the risk and benefit ratio for the participant
  • Presence of high-risk comorbidities
  • Investigations and tests imposing in-person visits vs possibility of using local facilities
  • Access to experimental treatment (hospital vs home (oral treatment))
Factors Worsening the Situation for Rare Cancers
• Expertise required for diagnosis → ↑↑ delay
  • Decline in diagnosis > common cancers

• Critical in absence of standard of care

• Research programs deprioritized given the urgency of developing vaccines & therapies for infected patients.

• National research efforts & local organization redirected to COVID-19

• Research programs deprioritized given the urgency of developing vaccines & therapies for infected patients.

• Access to experimental treatment

Diagnosis

Change in trial programs

Reprioritization/ repurposing

Rare Cancers
Adapting Clinical Research
### European and National Policies

#### Regulatory Bodies
- Regulatory guidelines by EMA (European Medicines Agency) and FDA (Food and Drug Administration)

#### National Policies
- Implementation of preventive strategies changing over time (lockdown policies, travel restrictions, social distancing, …)

#### Mitigation plan of Health Care Facilities
- Prioritization of activities
- Reorganization of infrastructures

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More flexibility for the recruitment and the follow-up of patients in trials
During the Crisis: Flexible arrangements!

**Scientific**

- Realtime Guidance (study procedures, treatment, reporting of serious toxicities) provided to participating sites
- Collect of information from National and European Regulators
- Adaptation of the ongoing trials → amendments approved by the Competent Authorities and Ethical Committees
- Collect of deviations related to the pandemic, flagging relationship with COVID-19.

**Operational**

- For study procedures (tolerance to experimental treatment, well being), involvement of local facilities (laboratory, imaging procedures), window of assessments extended.
- Physical visits → virtual visits
- e-consent process
- Ship oral drugs directly to patients
- Remote on site visits from the Sponsor

Resources: when possible homeworking
Impact on Researchers
Impact on Researchers

The UK Research and Innovation’s survey on researchers, conducted between February and March 2021, shows that the pandemic did affect:

» Research
» Mental health
» Future career prospects.
<table>
<thead>
<tr>
<th>Researchers (%)</th>
<th>Negative impact</th>
<th>Positive impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>61</td>
<td>Research time</td>
<td></td>
</tr>
<tr>
<td>58</td>
<td>Research planning</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>Work activities (teaching, administrative tasks)</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td></td>
<td>Unexpected opportunities</td>
</tr>
</tbody>
</table>
Lasting Changes for Clinical Research
Given the pandemic and the multiple waves in 2020 and 2021, did the enrollment remain low?

**Used data:** Initial enrollments to clinical trials conducted by the SWOG Cancer Research Network (important academic research group in USA) extracted from research program conducted between January 1, 2016, and February 28, 2021.

Total participants = 29,398

- During the pandemic, actual enrollments were 77.3% of expected enrollments.
- With marked reduction for trials focusing on prevention
- Regarding trials focusing on treatment they were less affected

Participation in Clinical Trials

Will patients be as willing to participate in clinical research as before the outbreak?

» In the USA, a survey has been conducted with 3054 participants between May 27, 2020 and June 17, 2020. A total of 933 responses (30.6%) were received.

» Among respondents, the majority (79.5%) indicated no difference. However nearly one-fifth of patients with cancer reported that they would be less likely to participate in a trial:

High rates of COVID-19 infection → ↓ willingness

With the rapid development and implementation of clinical trials designed to research COVID-19 → room for improving clinical research in the interest of the community.
Post Crisis: New Model of Collaboration

» Get inspired by the model of collaboration between competitors, regulators and academia used for the accelerated development of vaccines and therapies for COVID-19
Flexible and creative adaptation

» Adopting new working practices < lessons about modifications of trials during the crisis

• The adaptation of existing processes particularly for facilitating the continuation of research:
  • Streamlining data collection (essential ones) and operational processes related to trial management
  • Flexibility for drug delivery
  • Homeworking for research staff (productivity, satisfaction, retention)

» Reducing patient visits

• The use of telemedicine (patient’s safety, remote management)
  • such as phone calls, video calls

» Digitalising research processes

• Increased involvement of technologies to ease data capture
• Implementation of
  • e-consent process
  • e-signatures for trial documents
  • Electronic submission for regulatory process if not already in place

Thank you!