EPTRI
European Paediatric Translational Research Infrastructure

EPTRI SCIENTIFIC MEETING

BOOK OF ABSTRACTS

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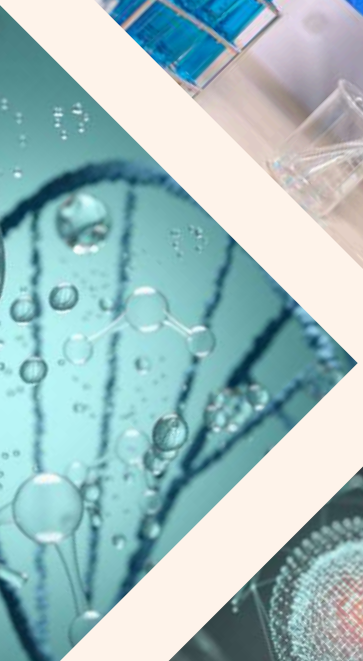

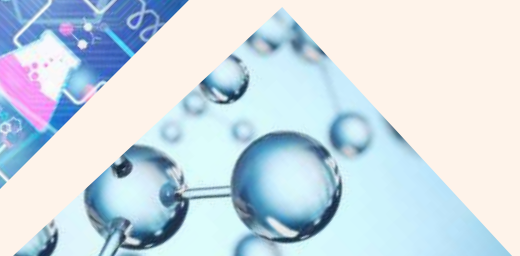

“The Challenge of Paediatric Research”

SPEAKER SECTION

SPEAKER: VIVIANA GIANNUZZI

Challenges and opportunities for paediatric research from the new proposed EU rules

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In the paediatric field, non-profit research has always played a key role in advancing knowledge and evidence-based resources.
Over the past twenty years, the EU Paediatric Regulation (EC) 1901/2006 has established a system of obligations, incentives and rewards to stimulate the Research and Development (R&D) of medicines for children.
Currently, the Paediatric Regulation is being revised as part of the ongoing revision of the General EU Pharmaceutical legislation aimed at improving the availability and access to effective and affordable medicines, including those for children and rare disease patients. In this context, the European Commission has proposed a regulation and a directive that are in the hands of the European Council.
Among the proposed rules, the ones that would more greatly impact on the paediatric no-profit research deal with: unmet medical needs identification, repurposing, mechanism of action criteria for Paediatric Investigation Plans (PIPs), possible simplification of the PIP procedure, hospital exemptions for advanced therapies, participation in EMA activities.
As an example, multi-stakeholder actions have been proposed to identify unmet medical needs, even if no paediatric-specific provisions have been proposed, in contrast with the current applicable provisions of the Paediatric Regulation. Moreover, the opportunity for non-profit entities to present data for authorising therapeutic indications will demand researchers to liaise with regulatory authorities and possibly turn off-label to approved uses. Academia will also expect to contribute to identifying paediatric conditions potentially targetable by a drug based on its mechanism of action.
In conclusion, the proposal to revise the EU pharmaceutical legislation is promising for EU citizens and for special populations, like children. The proposed changes in the regulatory pharmaceutical landscape will affect paediatric research and academia will be demanded to strengthen its regulatory expertise to participate in the R&D of paediatric medicines.

SPEAKER: RICCARDO MASETTI

The gut microbiome in paediatric stem cell transplantation: challenges and perspectives

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Background: FMT has become the standard of care for Clostridium difficile resistant infections and has been explored for other indications in the field of hematopoietic stem cell transplantation (HSCT). Indeed, in this setting it has been used to treat steroid refractory (sr)-GvHD (Malard F, 2023) as well as to decolonize patients carrying a MDRO (Battipaglia G, 2019). Additionally, microbiota diversity before HSCT has been associated with transplant outcome both in adults (Peled J, 2020) and children (Masetti R, 2024). Despite increasing use, FMT has been rarely performed in pediatric hematologic patients; here, we report the experience of 3 Italian centers.

Methods: we collect data of all pediatric patients receiving a FMT in 3 pediatric Italian centers (Roma, Bologna and Padova) for one of the 2 indication: i) sr-GvHD or ii) decolonization of MDRO (in this case, as additional inclusion criteria, the patient had to be scheduled or had already received an allogeneic HSCT).

Results: 28 patients were included, with a median age at FMT of 4,0 years (range 0.8-18.6), 16, 9 and 3 from Rome, Bologna, and Padova, respectively. The indication for allo-HSCT was oncologic disease in 20 and non-oncologic in 8. The donor was HLA-identical sibling in 6, haploidentical family member in 11, matched unrelated donors in 9 and cord blood in 2 cases. Stem cell source was Bone Marrow in 50%. Eighteen patients received FMT for eradication of MDR germs, 5 for treatment of intestinal SR-GvHD, and 5 for both indications. A total of 45 infusions of FMT were performed (median of 1/patient, range 1-4), via upper digestive tract, using endoscopy in 17 patients, a naso-jeujenal tube in 9 and percutaneous endoscopic jejunostomy in 2. In all cases, an unrelated fecal donor was selected, with frozen material employed in 93% of patients. No severe adverse events were observed following the procedure, 5 patients reported grade I-II adverse events (abdominal pain, nausea, SIRS) (Table 1). Regarding eradication of MDR bacteria, 14 received FMT pre allo-HSCT, while 9 a median of 263 days post-transplantation (range 55-487). The decolonization rate was 74% and 50% at 1- and 6-weeks post FMT, respectively. Ten patients received FMT for the treatment of intestinal SR-GvHD, after a median of 4,5 lines of treatment (range 3-7). The overall response rate and Complete response rate at 14 days after FMT were 80% and 50%, respectively, while at 28 days after FMT they were 78% and 67% (Figure 1). Metagenomic analysis in a subset of patients undergoing FMT for intestinal SR-GvHD showed a progressive increase in alpha diversity, with reduction in pathobionts and increase in commensals after the fecal infusion.

Conclusions: FMT was found to be a safe and well-tolerated procedure in children undergoing allo-HSCT with an encouraging rate of decolonization from MDR and remission of SR-GvHD.

SPEAKER: TIMOTHY CHOU

Paediatric Moonshot – Accelerating Global Paediatric Translational AI Research

Many don't realize that 60% of rural U.S. counties lack pediatric expertise. Three states have no pediatric emergency physicians. While the U.S. has 3,000 pediatric cardiologists, none serve rural counties; globally, there are only 300 in India and just one in Rwanda. Yet, we have the technology to build AI applications for cardiology, orthopedics, oncology, radiology, and emergency medicine—bringing expert-level diagnostics and treatment to underserved communities.

All childhood diseases are rare diseases. Take focal cortical dysplasia (FCD), a rare brain lesion that, if untreated, causes epileptic seizures. A teenage boy has suffered 2-3 seizures per night for over a decade. His early MRI scans showed nothing, leading to years of ineffective drug treatments. Recently, a new MRI scan suggested he has FCD—an operable condition that could cure him for life. The challenge? While 25,000 FCD cases occur annually in the U.S., no pediatric neuro-radiologist sees enough cases to become an expert. But AI could change that. By accessing MRI images worldwide, we can train an AI model to diagnose FCD in real-time on any MRI machine, offering hope for a future with improved diagnosis processes.

Trustworthy, privacy-preserving, real-time AI applications deployed at the point of care are the only systemic way to reduce healthcare inequity, lower cost and improve patient outcomes across the world.

While centralized infrastructure has driven the rise of consumer AI applications (e.g., ChatGPT), **centralized infrastructure will not work for AI in healthcare and life sciences**. The data sizes are much larger, the demands for privacy much higher and the need for real-time results much greater.

Advancing AI in healthcare requires data. Unlike other software, reliable, accurate non-biased AI applications cannot be built without large quantities of diverse data. That data is in the building of hospitals, clinics and research labs across the world. Real-time data is in the clinical machines (ultrasound, EKG, bedside monitor). Real time data is in the research machines (sequencers, mass spectrometers) and offline data is available in the PACS and EMRs.

Launched out of Stanford University, BevelCloud has engineered **a secure, privacy-preserving distributed AI cloud infrastructure**. Rather than move the data to the AI application move the AI application to the data in the building. This infrastructure enables moving AI research work from the bench to the bedside.

We are building a Distributed AI Lab for Healthcare and Life Sciences to provide authorized applications with access to real-time data from all imaging machines, as well as offline data from PACS and EMRs. The Lab when completed will encompass 32 sites, over 3000 distributed servers as well as access to over 2,000 TB of real-time imaging data (CT, MRI, Ultrasound, Xray, PET) as well as all PACS and EMR data. We will use distributed, federated, swarm learning technology to **translate 100+ deep learn research applications from the bench to the bedside**. See appcommons.bevelcloud.ai for examples.

While we've primarily focused on machine-generated data—especially imaging data—but there's also valuable text data within PACS and EMRs. By engineering digital twins for PACS and EMRs, we've enabled seamless data access. Now, with the ability to deploy an in-the-building LLM (e.g., DeepSeek, LLaMA3…), we're opening doors to an entirely new class of applications.

Here are three groundbreaking projects we're working on all focused on text data.

Total Recall: A Patient Agent

A local LLM trained on medical records offers "total recall." Andy Guinigundo, Director of Precision Oncology at Cincinnati Cancer Advisors, says, "It's like a patient with perfect recall." Queries work via text or voice in any language. We're scaling this tech across hospitals to boost productivity, especially for infusion nurses and pre-visit summaries. Deployed on BevelCloud's distributed AI infrastructure.

Distributed AI Clinical Trial Matching

The goal: Answer, "What trials is Jane Smith eligible for?" Matching patients to trials requires analyzing massive data—EMR records (up to 3,500 pages) and drug protocols (300+ pages). Our multi-AI system enables an EMR-based agent to interact with a protocol agent to determine eligibility. The EMR stays in-hospital, and drug protocols remain secure within biopharma firewalls.

Zero-Cost Labeling: AI for Medical Imaging

Deep learning in medical imaging needs labeled data, but specialists lack time, and interns lack expertise. We're automating labeling using PACS digital twins—leveraging expert-authored PACS reports as the primary data source. This approach cuts costs and speeds up high-quality medical image labeling.

We're excited about the future of AI in healthcare. If you're interested in collaborating or learning more, reach out!

SPEAKER: MAREK MIGDAL

The Birthday of EPTRI AISBL

Marek Migdal[1,2]

1 – EPTRI; 2 - Children's Memorial Health Institute, Warsaw, Poland

The European Paediatric Translational Research Infrastructure (EPTRI) started as a European funded initiative, coordinated by Consorzio per Valutazioni Biologiche e Farmacologiche (CVBF) arising from the need to find answers to the serious lack of medicines for children. As of March 4th, 2024, it has been established as a non-profit research organization incorporated in the form of an Association Internationale Sans But Lucrative (AISBL) governed by Belgian law, based at Leuven University. EPTRI AISBL consists of 18 members representing 9 different countries, bringing together a diverse range of expertise and institutions dedicated to paediatric research and innovation. It promotes various initiatives, including the publication of The EPTRI Manifesto on Paediatric Research, EPTRI surveys, and a toolkit. Additionally, a one-year online educational program has been developed to support paediatric research.

EPTRI AISBL is organized as a distributed Research Infrastructure according to a Hub and Spoke model, composed of several research units grouped within Thematic Research Platforms - TRPs (according to their area of expertise) and National Nodes (according to their location), and is governed through well-defined statutes and internal procedures, where the General Assembly and the Board of Directors oversee strategic decisions, while the CMO is responsible for implementing these decisions and managing the daily operations of EPTRI AISBL.

It provides paediatric research services in five technical and scientific domains focusing on paediatric medicines discovery, biomarkers and biosamples, developmental pharmacology,

paediatric medicines formulations, paediatric medical devices. Additionally, upcoming TRPs will focus on advanced therapy medicinal products and digital health technology. These TRPs offer integrated, cutting-edge services to advance paediatric research in the development of medicines, devices, and technologies. A transversal platform delivers centralized services to support all stages of paediatric research in the basic, pre-clinical, and translational settings. EPTRI AISBL fosters an open science environment, removing geographical, institutional, and financial barriers to innovation in paediatric research.

EPTRI AISBL is a member of several key partnerships, including Enpr-EMA (Category 3), supporting paediatric drug development and clinical trials; the European Open Science Cloud (EOSC), enhancing collaboration, data sharing, and digital innovation; the EU Health Coalition, advocating for paediatric research in health policies; and the European Alliance for Transformative Therapies (TRANSFORM), contributing to regulatory improvements.

EPTR AISBL has been involved in a European funded project, Orphadev4kids with the aim to implement a complex innovation ecosystem in the orphan and paediatric medical devices field by supporting academy, research centres and SMEs that invest on paediatric devices development. With specific objectives are to provide access to a paediatric MDs Platform for users needing dedicated research and development services, establish a comprehensive ecosystem that includes tools, facilities, and support services, and develop three case studies focusing on osteogenesis imperfecta and cyanotic congenital cardiac diseases.

EPTRI AISBL's future directions included its application for the European Strategy Forum on Research Infrastructures (ESFRI) 2026 Roadmap, with the goal of being recognized as a European Research Infrastructure. The application focused on advancing ATMPs, expanding the use of MDs beyond diagnostics to include other paediatric applications, emphasizing digital health applications, and developing an innovative clinical research platform to support cutting-edge methodological approaches.

EPTRI AISBL continuously maps paediatric expertise and competencies across EU and non-EU countries through online surveys to identify potential service providers and invites organizations to join EPTRI AISBL by completing and submitting the Association Form to coordinator@eptri.eu, with the aim of advancing knowledge on human development and ontogeny and supporting the discovery of new therapies and devices for children.