IPOPI 4TH REGIONAL ASIAN PID MEETING

19-20 NOVEMBER 2022

KUALA LUMPUR, **MALAYSIA**

an **IPOPI** event

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GLOBAL ALLIANCE EDUCATIONAL SEMINAR

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Takeda

SCID Newborn screening: experience from France

Martine Pergent

4th IPOPI Asian regional meeting

Kuala Lumpur, 19 November 2022

Newborn screening in France

- Newborn screening in place since 1972
  - Phenylketonuria (PKU)
  - Congenital hypothyroidism;
  - Congenital adrenal hyperplasia;
  - Cystic fibrosis ;
  - Medium-Chain-Acyl-CoA Dehydrogenase (MCAD) deficiency;
  - Sickle cell disease (in populations at risk).

DEPISTREC: a prospective study*

- Background
  - After it was demonstrated in 2005 that T cell receptor excision circle (TREC) quantification for dried blood spot (DBS) samples on Guthrie cards is an effective means of SCID screening and following several pilot studies, the practice was formally recommended in the US in 2010.
  - In France, before the health authorities could recommend adding SCID to the list of diseases that were routinely screened for, feasibility and cost-effectiveness studies had to be conducted with a sufficiently large cohort of neonates.
- The prospective study aims to study:
  - the feasibility of generalized neonatal screening for SCID in France,
  - its clinical and health economic utility and cost-effectiveness ratio.
  - it will seek to show that generalized neonatal screening for SCID is feasible and acceptable to the population.

DEPISTREC: a prospective study*

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  - In France, before the health authorities could recommend adding SCID to the list of diseases that were routinely screened for, feasibility and cost-effectiveness studies had to be conducted with a sufficiently large cohort of neonates.
  - We carried out three such studies:

    The first sought to verify the effectiveness of the assay.

    The second, DEPISTREC, evaluated the feasibility of universal SCID screening in France and assessed the clinical benefit and economic advantage it would provide.

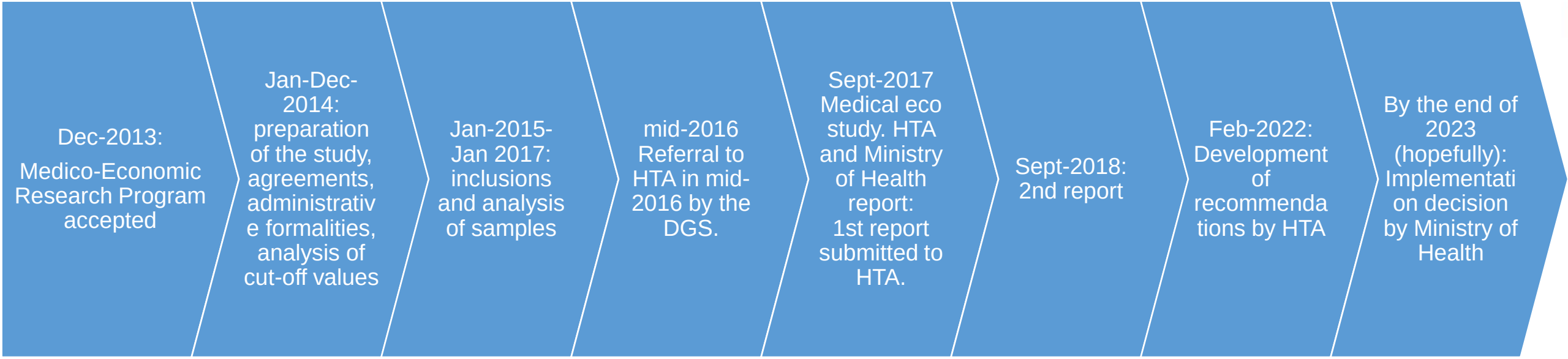
    The third study, NeoSKID, has been offering SCID screening in the Pays de la Loire region of France.

    This review briefly describes routine newborn screening (NBS) and management of primary immunodeficiency diseases (PIDs) in France, and then considers the lessons from our studies and the status of SCID screening implementation within the country.acceptable to the population.

- Neonatal screening for severe combined immune deficiency: Presentation of the DEPISTREC study

C.Thomas[a] S.Mirallié[b] C.Pierres[c] C.Dert[c] N.Mahlaoui[d] M.Audrain[e] groupe DEPISTREC[f1]

Depistrec: 2013-2023



New algorithme in case of positive screening

Positive screening:
TREC<11 copies in Full-term newborns
Or TREC≤5 copies in Premature newborn

Visit to a paediatrician

Positive screening (Premature newborn)
(5<TREC<21 copies)
Or Positive screening (Full-term newborn)
(10<TREC<21 copies)
Or Inconclusive results
(TREC<21 copies and b-actin <35 copies

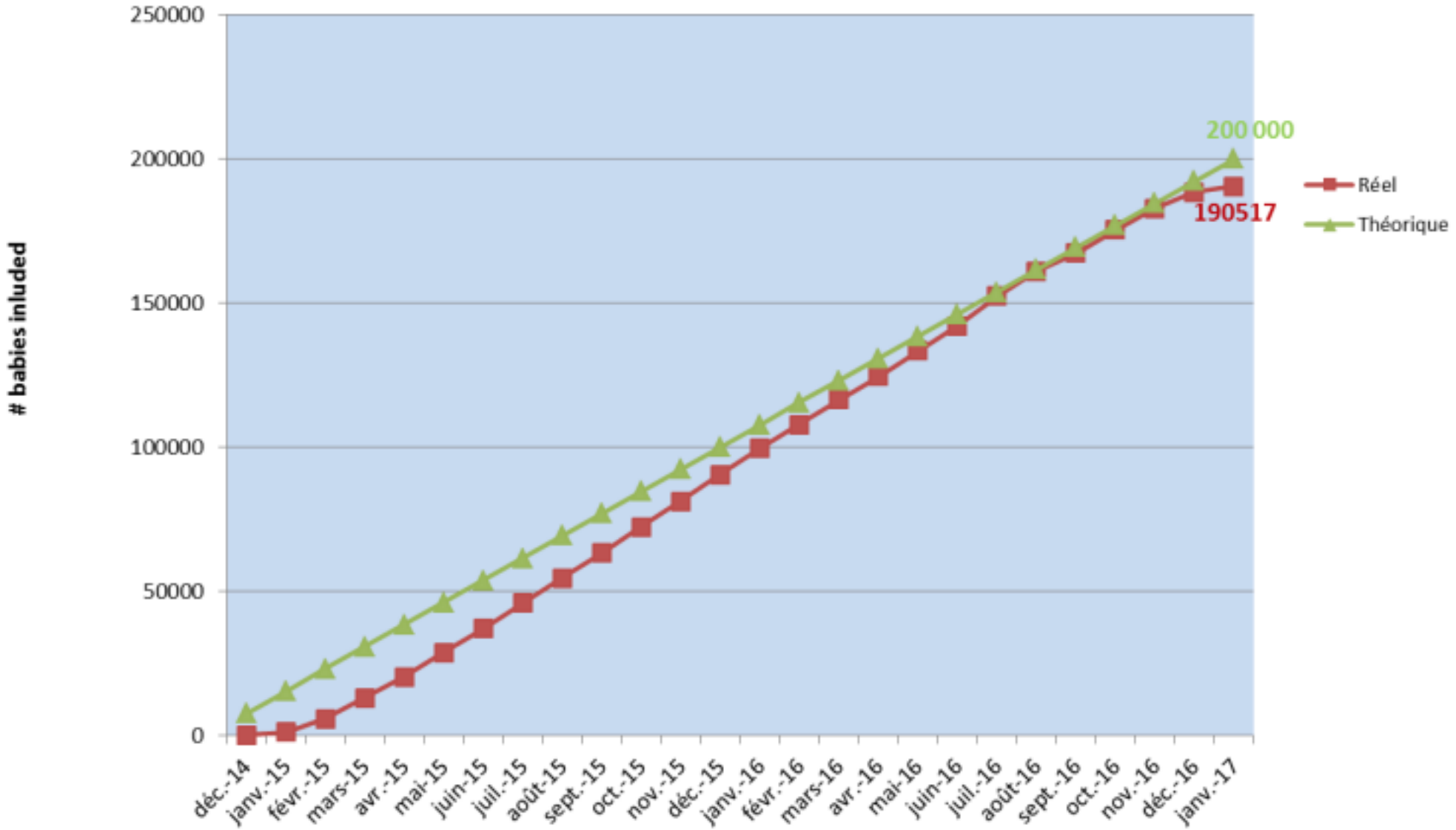
New card

Negative
Stop

Still positive or Inconclusive
(TREC<21 copies)

Visit to a paediatrician

Inclusion curve



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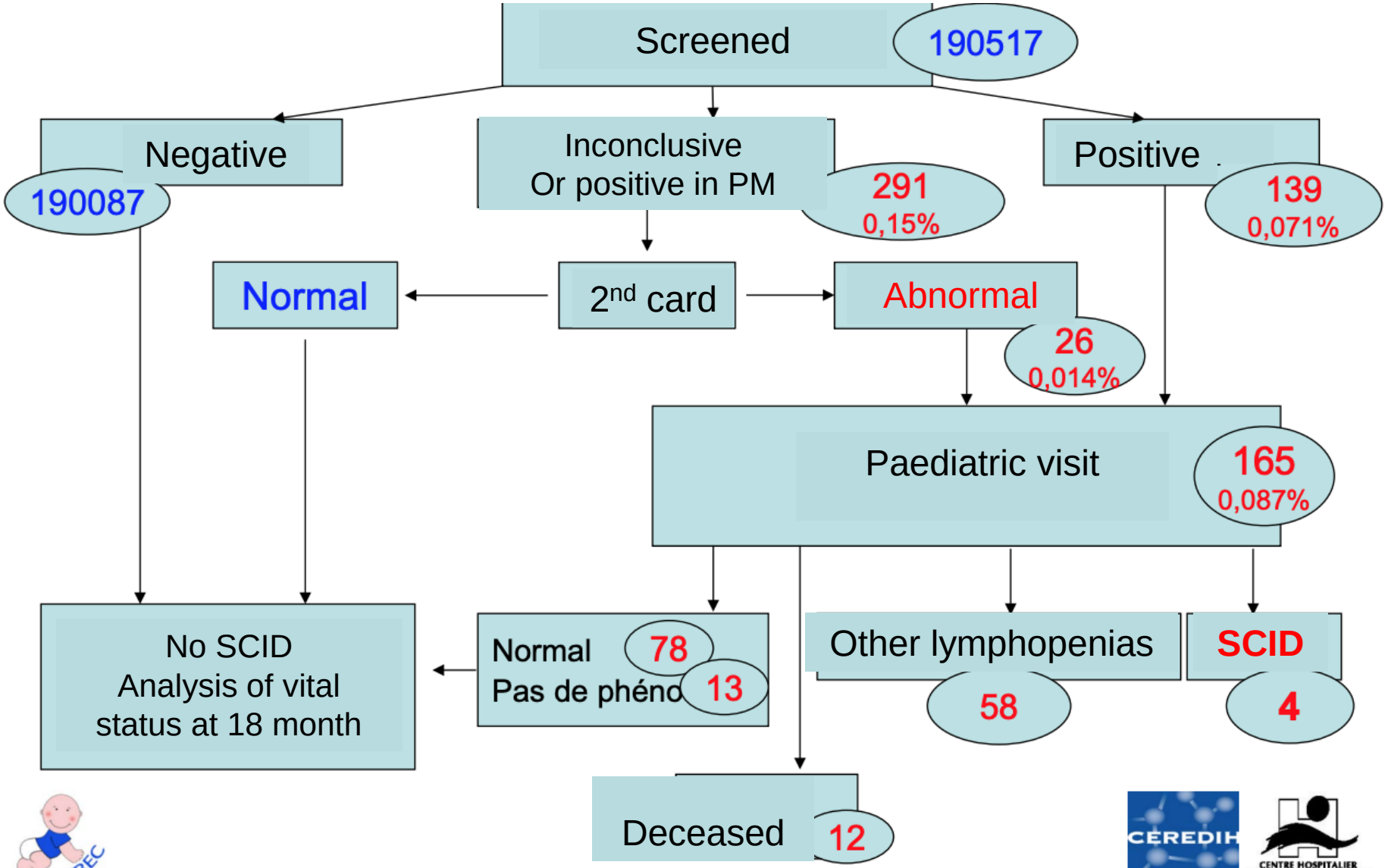
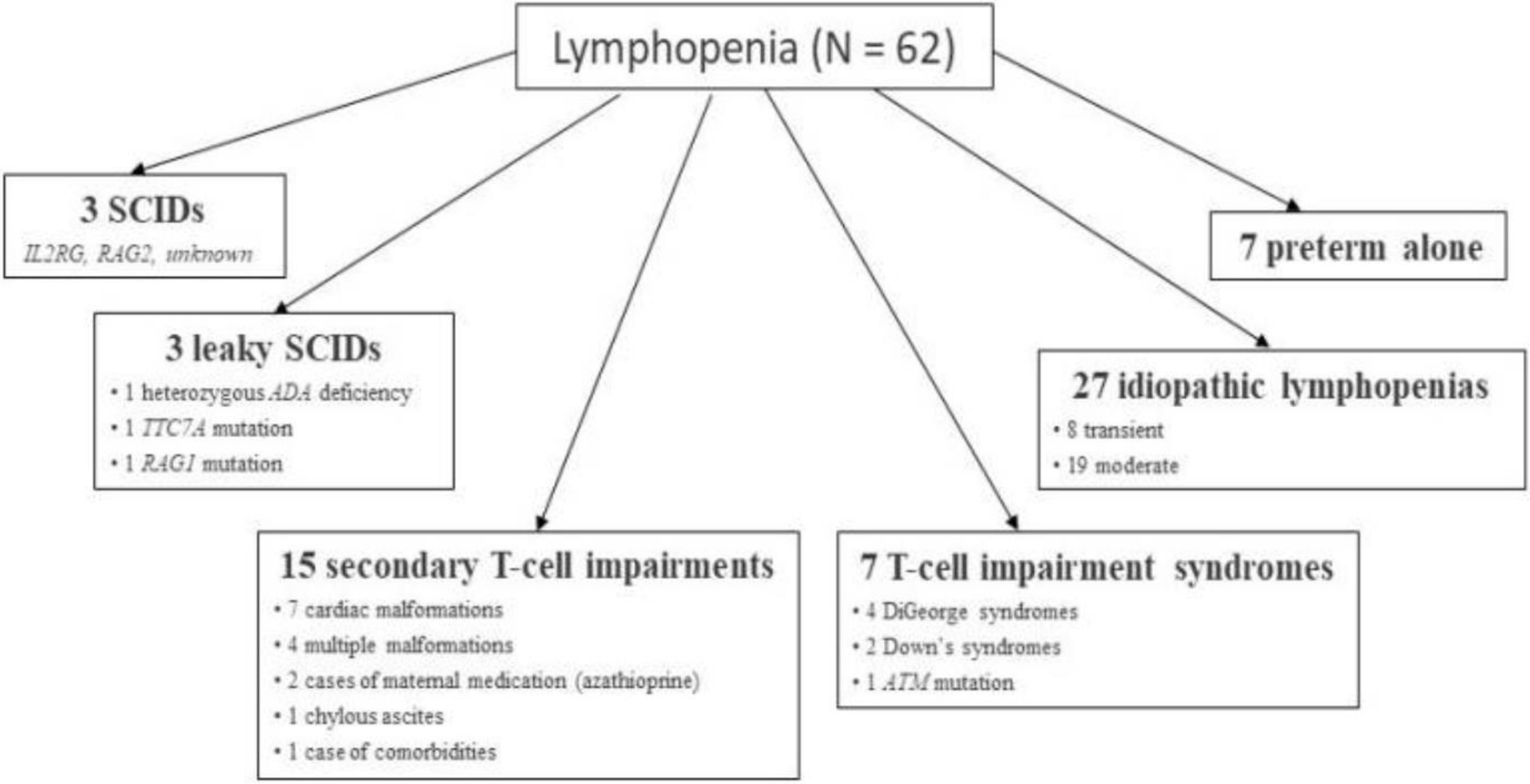
Analysis


Screened
190517
Negative
190087
Inconclusive
Or positive in PM
291
0,15%
Positive
139
0,071%
Normal
2nd card
Abnormal
26
0,014%
Paediatric visit
165
0,087%
No SCID
Analysis of vital
status at 18 month
Normal
78
Pas de phéno
13
Other lymphopenias
58
SCID
4
Deceased
12


Lymphopenia (N = 62)
3 SCIDs
IL2RG, RAG2, unknown
3 leaky SCIDs
• 1 heterozygous ADA deficiency
• 1 ITC7A mutation
• 1 RAG1 mutation
15 secondary T-cell impairments
• 7 cardiac malformations
• 4 multiple malformations
• 2 cases of maternal medication (azathioprine)
• 1 chylous ascites
• 1 case of comorbidities
7 T-cell impairment syndromes
• 4 DiGeorge syndromes
• 2 Down's syndromes
• 1 ATM mutation
27 idiopathic lymphopenias
• 8 transient
• 19 moderate
7 preterm alone

Depistrec lessons learnt

- Feasibility and Clinical Utility
  - Screening for SCID is both feasible and effective and offers the added benefit of detecting severe T cell lymphopenia in children with non-SCID disorders such as DiGeorge syndrome, Down syndrome, ataxia-telangiectasia, and congenital heart diseases or syndromes
  - Test validation rules must be clearly defined and the decision-making algorithm leading up to diagnosis and treatment standardized, so that every child has the same chances regardless of where they are born.

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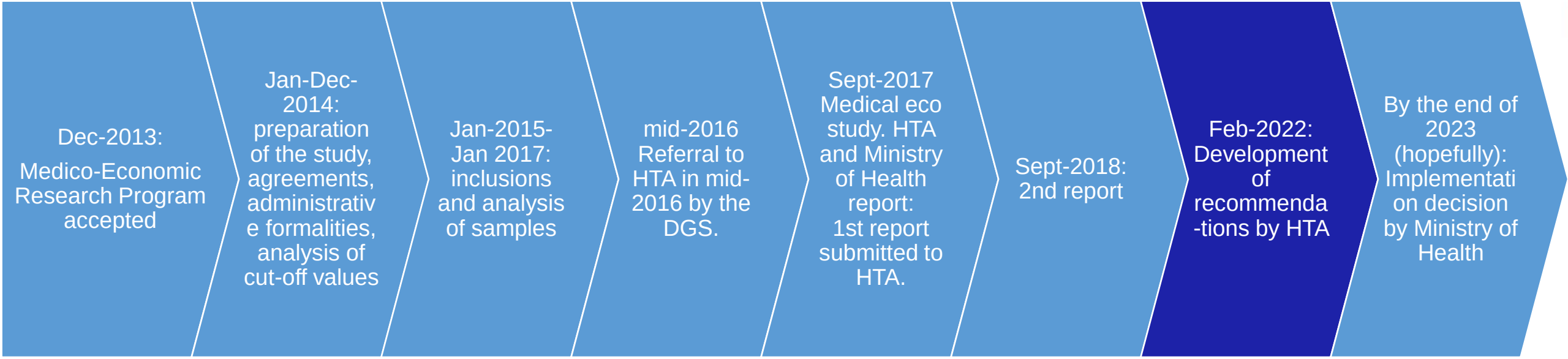

HTA recommendation (Feb 2022)

- HAS recommends to extend universal newborn screening to SCIDs by TRECs quantification in the general population because:
  - the severity of the SCIDS;
  - the vital issue of early diagnosis and rapid treatment before the onset of infections;
  - the existence of a reference treatment;
  - and the availability of a recognized screening test.

- **under certain conditions.**
  - SCID NBS to be conditioned to a compulsory assessment after 5 years, and regular intermediate assessments
  - Screening can only be set up, even under conditions, if all steps leading to HSCT aim to ensure it is done by two months after birth.
  - The necessary to ensure that this national programme is applicable, that pathways are harmonised and streamlined, nationwide, to prevent inequality between regions.

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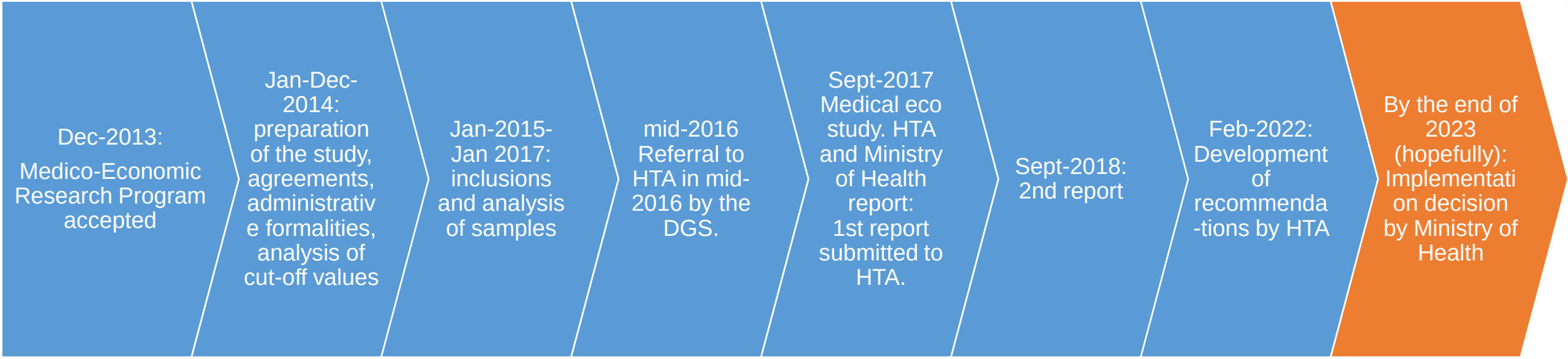

Un grand merci à tous !

CHU Nantes :
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-Dr S. Mirallié, dépistage,
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-Dr M. Audrain, laboratoire d'immunologie

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-E. Divry, labo dépistage,

Les Enfants,
Les Parents

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- **Médico-économiste** (URC-ECO AP-HP) : Pr I.Durand-Zaleski,

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-**Maternités**

-**Pédiatres**

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