Poster # 804

Conference on Retroviruses and Opportunistic Infections CROI 2018

Mar 4-Mar 7, 2018

Boston, Massachusetts

Does changing ART in early pregnancy for fetal risks destabilize viral suppression?

Violaine Peyronnet Chabrier[1,2], Josiane Warszawski[1,3,4], Jeanne Sibiude[1,2,5], Catherine Dollfus[6], Christine Rouzioux[7,8], Jérôme Le Chenadec[1], Albert Faye[5,9], Roland Tubiana[10], Laurent Mandelbrot[1,2,5] for the ANRS CO1-French Perinatal Cohort Study

[1]CESP INSERM U1018, Le Kremlin-Bicêtre; [2]AP-HP Hôpital L. Mourier, Colombes; [3]Univ Paris Sud, Le Kremlin-Bicêtre; [4]AP-HP Hôpital Bicêtre, le Kremlin-Bicêtre; [5]Univ Paris-Diderot, Paris; [6]AP-HP Hôpital Trousseau, Paris; [7]AP-HP Hôpital Necker-Enfants Malades, Paris; [8]Univ Paris-Descartes, Paris; [9]AP-HP Hôpital R. Debré, Paris; [10]AP-HP Hôpital Pitié Salpétrière, Paris, FRANCE

EPF

INSERM CESP 1018 - Hôpital de Bicêtre AP-HP
82 rue du Général Leclerc
94276 LE KREMLIN BICETRE Cedex
Tél. : 33 1 49 59 53 05/10 Fax : 33 1 49 59 53 00

Corresponding authors:
V. Peyronnet (violaine.peyronnet@inserm.fr)
J. Warszawski (josiane.warszawski@inserm.fr)
L. Mandelbrot (laurent.mandelbrot@aphp.fr)

OBJECTIVE

To determine whether changing ART in pregnant women on effective antiretroviral therapy at the time of conception because of concern about fetal risks leads to poorer control of viral load.

PATIENTS AND METHODS

The National French Perinatal Cohort (EPF, ANRS CO1/CO11) : Includes all pregnant women with HIV and their children since 1986 in 90 French centres. Covers about 70% of deliveries of HIV-infected women in continental France. CO1 component of cohort records detailed information during the pregnancy ; CO11 is simplified.

Study population:

Inclusion:
- Outcome at ≥ 14 weeks' gestation (WG) or more, from 2005 to 2015
- On ART at the time of conception

Exclusion:
- HIV-2
- EPF CO11: No details on indication of change and initial VL
- For the main outcome: exclusion if VL<14WG not available, VL>50cp/mL <14WG and patients who changed for inefficacy or for intolerance

Definitions:

•**Treatment switch:** addition, modification or deletion of at least one molecule in the ART combination used at the time of conception

•**Recommendations:** Recommended in pregnancy, Alternative or Not recommended, according to French National guidelines at the time of the pregnancy

•**Main outcome:** maternal viral load during the pregnancy and at delivery

•**Statistical analysis:** For factors potentially associated with a switch: logistic regression with multivariate models. For the potential impacts : multivariate logistic regression or survival analyses with Cox censored at the date of a second potential switch with adjustment on propensity score.

Table 1 –Proportion of treatment switch <14WG as a medical strategy according to the period and guidelines (EPF CO1)

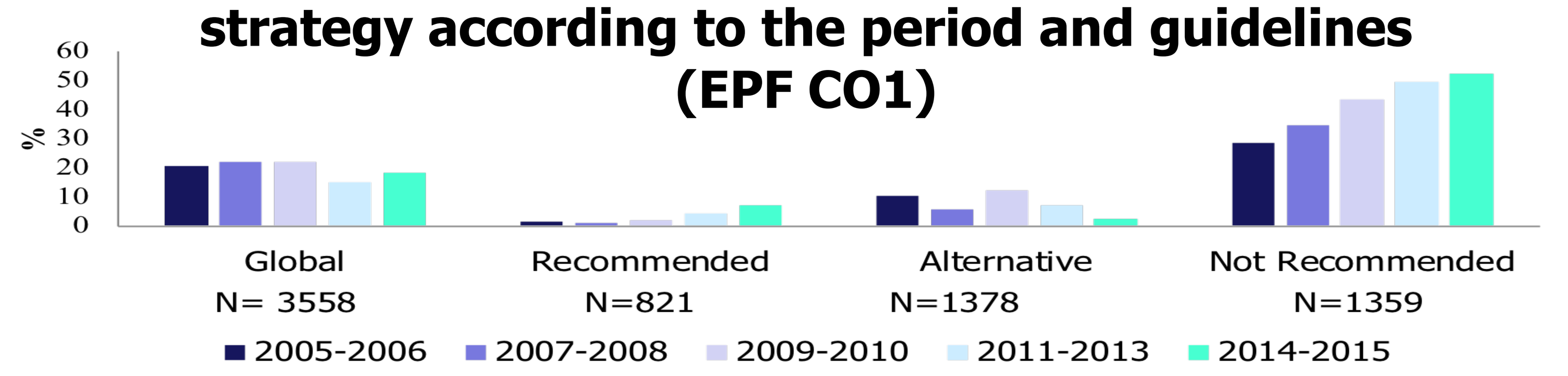

Fig 1 – Selection of study population

EPF Cohort (CO1/CO11) 2005-2015 N=10553

(CO1/CO11) HIV-1, on ART at the time of conception N=4983

Exclusion: **EPF CO11** (indication of change not given and VL<14WG not available) (N=1409)

EPF CO1 HIV-1 on ART N= 3574

Exclusion: **EPF CO1** with VL<14WG not available (N=1205)

VL <14WG available N=2369

VL< 50 copies/mL <14WG N=1820

Exclusion: Changed ART for **inefficacy** (N=23) Changed ART for **intolerance** (N=22)

Changed ART <14WG for medical strategy N= 411

No change or change after 14WG N = 1364

Table 2– Factors associated with an ART switch <14WG as a medical strategy. Multivariate analysis.

	Multivariates analysis (N=1655)		
	Adjusted OR*	IC95%	p
Treatment guidelines			
Recommended	1		**<0.01**
Alternative	**2.2**	**[1.3-3.7]**	
Not recommended	**23.1**	**[14.0-38.2]**	

*adjusted on previous pregnancies in EPF, study site, period, marital status, time from HIV diagnosis to pregnancy, professional status (propensity score)

Table 3 – Virological outcomes after a switch <14WG as a medical strategy. Multivariate analysis.

	Switch				Multivariate Analysis		
	No (N=1364)		Yes (N=411)		Ora[1]/ HRa[2]	IC 95%	p
	n	%	n	%			
VL>50 copies/mL during the pregnancy	212	15.6	79	19.3	**1.0[2]***	**[0.7-1.4]**	**0.9**
VL>50 copies/mL at outcome	58	4.6	25	6.5	**1.1[1]***	**[0.6-2.0]**	**0.7**

* adjusted on propensity score, [1] Cox model, [2] Logistic regression

Table 3 – Virological outcomes after a switch <14WG as a medical strategy, according to the type of recommendation. Multivariate analysis.

	Type of treatment																				
	Recommended (N=412)							Alternative (N=738)							Not recommended (N=647)						
	Switch							Switch							Switch						
	No (387)		Yes (25)		ORa[1]/ HRa[2]	IC 95%	p	No (677)		Yes (71)		ORa[1]/ HRa[2]	IC 95%	p	No (355)		Yes (315)		ORa[1]/ HRa[2]	IC 95%	p
	%	n	%	n				%	n	%	n				%	n	%	n			
VL>50 copies/mL during the pregnancy	15.3	58	8	2	**0.4[2]***	[0.0-2.9]	0.4	14.3	92	27.5	19	**1.6[2]***	[0.9-2.9]	0.2	18.7	62	18.4	58	**0.9[2]***	[0.6-1.4]	0.6
VL>50 copies/mL at outcome	3.9	14	4.0	1	**1.2[1]***	[0.1-9.4]	0.9	4.0	24	4.5	3	**1.1[1]***	[0.3-3.7]	0.9	6.7	20	7.1	21	**1.1[1]***	[0.6-2.1]	0.8

* adjusted on propensity score, [1] Cox model, [2] Logistic regression

RESULTS

Factors associated with a switch in early pregnancy :

- 66.4% of switches made in order to **conform with guidelines**
- The type of the treatment: as compared to Recommended first-line options (6.1%)
  - aOR: **23.1** [14.0-38.2] when initial treatment was **contraindicated** (48,7% of switches)
  - aOR: **2.2** [1.3-3.7] when treatment was an **alternative** (9,9%)

Virological outcomes:

- No association between switch for pregnancy-related concerns and virological escape (**19.3%** in the switch group vs **15.6%**, HRa: **1.0** [0.7-1.4])

CONCLUSION

- Changing antiretroviral therapy <14WG for medical strategy **did not compromise viral suppression** in this population and period
- Multidisciplinary **preconceptional** care should be offered in order to anticipate with each woman which ARVs to use in pregnancy
- Further research is required on recent ARVs for **safety and risks**

ABSTRACT

Background : As increasing numbers of women with HIV are on becoming pregnant on antiretroviral therapy, and fewer infants are infected, there is concern about the possible risks for fetuses and infants exposed to ARV in utero. In case of potential toxicities or in the absence of good safety data, one option is to switch the maternal ART regimen as early as possible in pregnancy. Our aim was to study the frequency and reasons of such treatment changes and to determine whether they led to poorer virological outcomes.

Study Design : All pregnancies in women with HIV1 enrolled in the national multicenter prospective French Perinatal cohort (EPF) were included if delivery was between 01/2005 and 12/2015, at 14 gestational weeks or more and the mother was on antiretroviral therapy (ART) at conception with a plasma viral load < 50 copies/ml. The reasons for a switch in the antiretroviral regimen were analyzed according to treatment guidelines at the time of the pregnancy, and defined as for medical strategy in the absence of reported adverse events. Virological and pregnancy outcomes were studied by survival analysis censored at the time of ART switch (suppression or change of at least one drug) and by logistic regression adjusted for a propensity score established for each patient according to baseline characteristics.

Results : Of 10365 pregnancies with an outcome > 14 weeks' gestation, nearly half (N = 4983) were on antiretroviral therapy at conception, and of these 1019 (9.8%) had a treatment switch in the first trimester of pregnancy. For 66.4% of these switches, the reason was a medical strategy to follow treatment guidelines. The proportion of switch was statistically higher when initial treatment was contraindicated (OR adjusted: 23.1 [14.0-38.2]) or was regarded as an alternative (ORa: 2.2 [1.3-3.7]), as compared to recommended first-line options. Treatment switches for medical strategy did not lead to poorer virological control, compared to pregnancies without such switches (19.3% vs. 15.6%, HRa: 1.0 [0.7-1.4]).

Conclusion : Changing antiretroviral therapy early in pregnancy with the goal of improving fetal and pregnancy outcomes did not appear to have a destabilizing effect on viral suppression. However, the impact may differ according to the specific regimens and patient characteristics. Multidisciplinary preconceptional care must be provided to women with HIV, as well as further research on recent antiretroviral drugs to document their safety and risks.

Thank all the centers participating in the French Perinatal Cohort: APHP Hôpital Louis Mourier, Colombes, France (Laurent Mandelbrot, Catherine Crenn-Hebert*, Corinne Floch-Tudal*, Fabienne Mazy, Marine Joras, Françoise Meier, Emmanuel Mortier, Catherine Briquet, , Houria Ichou, Laurence Marty, Hélène Jabbarian); APHP Hôpital Beaujon, Clichy, France (Pierre-François Ceccaldi*, Maïa Banige, Agnès Villemant Uludag, Virginie Zarouk, Agnès Lefort, Mariam Ben Salah); Hôpital Sainte Musse, Toulon, France (Gilles Hittinger*, Jean-Marc Chamouilli, Christian Burle, Alain Lafeuillade, Gisèle Philip,Véronique Lambry); CHG Marechal Joffre, Perpignan, France (Marie Medus*, Germaine Bachelard, Martine Malet); CHU Caremeau, Nîmes, France (Joëlle Dendale-Nguyen*); CHD les Oudairies, La Roche sur Yon, France (Thomas Guimard*, Karine Guimard, Jean-Pierre Brossier, Philippe Perré, Jean-Luc Esnault, Olivier Aubry, Sophie Leautez-Nainville, Valerie Bonnenfant, , Laeticia Laine); Centre Hospitalier William Morey, Châlon sur Saone, France (Sandrine-Anne Martha*, Elise Maurel, Michel Françoise, Muriel Barat, Patricia Murger); Centre Hospitalier, Vernon, France (Mahfoud Rouha*, Marc Lévy, Philippe Lumbroso, Alain Checoury, Osseni Sahadatu, Johnson)); Centre Hospitalier Intercommunal de Cornouaille, Quimper, France (Pascale Perfezou*, Gilles Blondin, Jean-Charles Duthé); Centre Hospitalier Universitaire, Brest, France (Séverine Ansart*, Luc De Saint Martin*, Philippe Le Moine, Jean-Charles Duthé); Centre Hospitalier, St Brieuc, France (Corinne Daniel*, Christian Calvez, Emmanuelle Boutaric, Jennifer Rohan); Centre Hospitalier Universitaire, Rennes, France (Cédric Arvieux*, Estelle Bauville, Christelle Dupre, Pascal Lotton, Enora Ouamara-digue); Centre Hospitalier Bretagne Atlantique, Vannes, France (Yves Poinsignon*, Marie Goussef, Anne Grelier, Gaetane Mousset, Corinne Cudeville, Virginie Mouton-Rioux); Centre Hospitalier de Bretagne Sud, Lorient, France (Mathilde Niault*, Isabelle Belzic, Philippe Moreau, Marie-Françoise Le Coz, Odile Lucyx Vaillant, Anne Guerin-Duplessy, Virginie Mouton-Rioux, Philippe De Morel); Centre Hospitalier de la région d'Annecy, Annecy, France (Virginie Vitrat*, Didier Tardif, Jacques Gaillat, Anne Vanderbergh, Suzanne Braig, Gaelle Clavere); Centre Hospitalier Intercommunal, Montfermeil, France (Marion Dehlinger-Paul*, Khaled Mohamed, Marie Echard, Michel Camus, Catherine Mulard, Marie-Agnès Fontelonga); Centre Hospitalier Intercommunal, Montreuil, France (Brigitte Heller-Roussin*, Cécile Winter, Marion Challier, Elise Debruyne); APHP Hôpital Cochin-Port Royal, Paris, France (Valerie Marcou*, Ghislaine Firtion, Emmanuelle Pannier*, Myriam Costa, Odile Launay, Dominique Salmon Ceron, Touria Belkacem, Youcef Bajawi, Valérie Raynal Aubret, Danièle Rivaux); APHP Hôpital Bichat, Paris, France (Sophie Matheron*, Neila Elaoun, Lahcene Allal, Sandrine Djoubou, Djamila Rahli, Agnès Bourgeois Moine, Morgane Valentin, Florence Damond, Virginie Huri, Valérie Vivier, Fatma Ait Yahia); Centre Hospitalier Intercommunal, Créteil, France (Valérie Garrait*, Isabelle Hau*, Claudine Touboul, Lanto Ratsimbazafy, Emilie Boiron, Brigitte Elharrar, Laurent Richier); Hôpital de la Croix Rousse, Lyon, France (Laurent Cotte*, Jean-Marc Labaune, René-Charles Rudigoz, Corinne Brochier, Valérie Galvan, Stanislas Ogoudjobi); Centre Hospitalier Pellegrin, pauchart, Bordeaux, France (Christophe Elleau*, Camille Runel-Belliard*, Thierry Pistone, Hervé Fleury, Jacques Horovitz, Boris Sandler, Denis Roux, Jean-Marie Ragnaud, Pierre Chabanier, Jean-Luc Brun, Sandrine Delveaux); CHU Les Abymes, Pointe à Pître, France (Blandine Muanza*, Mama Doufari Diallo, Isabelle Lamaury, Marie-Thérèse Sow, Ketty Samar); Centre Hospitalier Général, Creil, France (Bénédicte Carpentier*, Zafer Osman, Etienne Dienga); Centre Hospitalier Général, Longjumeau, France (Hervé Seaume*, Sarah Ducrocq, Philippe Bailly-Salin,Christelle Dusart Da Silva, Isabelle Fayolas); Hôpital Paule de Viguier, Toulouse, France (Julie Abbal*, Caroline Simon-Toulza*, Véronique Truillet, Noëlle Bogner, Julie Chiabrando, Evelyne Armand); Centre Hospitalier de la Côte Basque, Bayonne, France (Claudine Cayla*); Centre hospitalier intercommunal, Villeneuve St Georges, France (Anne Chacé*, Isabelle Matheron, Laurent Richier, Joe Miantezila, Sandrine Bry); Centre Hospitalier Intercommunal, Poissy Saint Germain en Laye, France (Sophie Couderc*, Catherine Narcy); Centre Hospitalier Général, Fontainebleau, France (Corinne Routier*, Rania Nassar); Centre Hospitalier Robert Ballanger, Aulnay, France (Marie-Anne Bouldouyre*, Ahmed Zakaria, Hélène Dauphin, Céline Goissen, Marie Belloy, Jean-Luc Delassus, Véronique Favret, Céline Nemeth); Hôpital Hautepierre, Strasbourg, France (MariaLuisa Partisani*, Natacha Entz-werle, Bruno Langer, Françoise Uettwiller, Myriam Durand) ; Hôpital Civil, Strasbourg, France (MariaLuisa Partizani*, Christine Cheneau, David Rey, Edith Ebel, , Patricia Fischer) ; Centre médico-chirurgical Obstétrique, Strasbourg, France (Eric David, Christophe Vayssiere, Michèle Weil, Marie Paule Schmitt, Israël Nisand) ; Centre Hospitalier Victor Dupouy, Argenteuil, France (Philippe Genet*, Dominique Brault, Christine Allisy, Juliette Gerbe, Virginie Masse, Bouchra Wifaq, Laurence Courdavault, Petra Gabor, Nathalie Tordjeman); APHP Hôpital Tenon, Paris, France (Marie-Gisèle Lebrette*, Lise Selleret, Déborah Samama, Geneviève Vaudre); Centre Hospitalier Général, Saint-Denis, France (Pascal Bolot*, Marie-Aude Khuong-Josses, , Mahdi Amel, Stéphane Bounan, Christelle Nourry, Sabine Andris); APHP Hôpital Necker, Paris, France (Stéphane Blanche*, Marine Driessen*, Pierre Frange, Florence Veber, Alain Fisher, Christine Rouzioux, Véronique Avettand-Fenoel, Nizar Malaoui, Marie-Christine Mourey); Centre Hospitalier Sud Francilien, Evry Corbeil, France (Michèle Granier*, Alain Devidas*, Anne-Claire Donnadieu, , Adrien May, Amélie Chabrol, Pierre Chevojon, Chahrazede Bellahcene, Audrey Sanchez, Claire Malbrunot, Joelle Neizelien, Nouara Agher); Centre Médico-Chirurgical et Obstétrical, Schiltigheim, France; CHR American Memorial Hospital, Reims, France (Claire Pluchart*, Christine Rouger); APHP Groupe Hospitalier Pitié Salpêtrière, Paris, France (Roland Tubiana*, Marc Dommergues, Manuela Bonmarchand, Luminata Shneider, Fabienne Caby, Ruxandra-Oana Calin, Christine Blanc, Catherine Lupin, michèle Pauchard); Centre Hospitalier René Dubos, Pontoise, France (Mohamed Amine Yangui*, Didier Roca, Darina Todorova, Juliette Laurent, A Ferry, Martine Deschaud, Laurent Blum); APHP Hôpital Béclère, Clamart, France (Véronique Chambrin*, Philippe Labrune*, Laure Clech, Mariem Raho-Moussa); Centre Hospitalier Marc Jacquet, Melun, France (Isolde Pauly-Ravelly*, Thierry Jault, Soufiane Bouabdallah, Lydie Sanchez, Anita Sanchez); Centre Hospitalier Général, Evreux, France (Ama Johnson*, Agnès Louchard, Claude Allouche, Jean Paul Pathe); APHP Hôpital Jean Verdier, Bondy, France (Eric Lachassine*, Laurence Benoist, Vincent Jeantils, Catherine Delannoy, , Amélie Benbara, Lionel Carbillon, Anne Borgne, Laurence Moreau, Fabienne Picard); Centre Hospitalier de Meaux, Meaux, France (Leïla Karaoui*, Véronique Lefevre Elbert, Valérie Balaz); CHU de l'Archet, Nice, France (André Bongain*, Fabrice Monpoux*, Anne Deville, Eliane Galiba); Centre Hospitalier François Quesnay, Mantes La Jolie, France (Ahmed Jabbar*, Martine Joutel); CHU Hôpital Nord, Amiens, France (Jean-Luc Schmidt*, Nathalie Decaux); Hôpital de la Conception, Marseille, France (Ludovic Cravello*, Katia Errichiello); CHU de Brabois-Hôpital des Adultes, Vandoeuvre les Nancy, France (Claire Hubert*); APHP Hôpital Trousseau, Paris, France (Catherine Dollfus*, François Hervé, Marie-Dominique Tabone, Mary-France Courcoux, Guy Leverger, Gilles Kayem, , Aurélie Schnurgier, Aurore Jensen, Geneviève Vaudre); Hôpital Charles Nicolle, Rouen, France (Didier Pinquier*, Alexis Gromez , Gaelle Pinto-Cardoso,); APHP Hôpital Robert Debré, Paris, France (Albert Faye, Constance Borie*, Martine Levine*, Sophie Matheron, Erianna Bellaton Marouts, Christine Boissinot, Marion Caseris, Virginie Pommelet, Geneviève Morau, Sandrine Leveille, Marie Astride Boumediene, Dominique Garion); APHP Hôpital de Bicêtre, Le Kremlin-Bicêtre, France (Delphine Peretti*, Corinne Fourcade*, Marie Houllier, Ikram Jrad, Katia Bourdic, Sylvie Monnier); CHU Hôpital Jean Minjoz, Besançon, France (Catherine Chirouze*, Aurélie Proust, Odile Catteau, Quentin Gardiennet); CHU de Nantes, Nantes, France (Véronique Reliquet*, Cécile Brunet-Cartier*, Norbert Winer, Edouard Vaucel, Audrey Rodallec, Elisabeth Garnier-André); CHRU Hôpital du Bocage, Dijon, France (Claire Briandet*); CHRU Hôpital Clemenceau, Caen, France (Jacques Brouard*, Pascale Goubin, Gaël Beucher, Julia Dina); Centre Hospitalier de Lagny, Lagny, France (Arnaud Chalvon Demersay*, Sylvie Tassi, Gaelle Lavarenne); Hôpital André Mignot, Le Chesnay, France (Mandovi Rajguru*, Fabienne Messaoudi, Nathalie Carre, Mandavi Rajguru, Claire Bobrie-Moyrand, Pierre Foucaudt); CHRU de Tours, France (Louis, Bernard*, Zoha Maakroun, Olivier Bourgault); Institut d'Hémato-Oncologie Pédiatrique, Lyon, France (Kamila Kebaïli*, Yves Bertrand, Véronique Alixe, Emeline Boyer); Hôpital Nord, Saint Etienne, France (Kareen Billiemaz*, Cécile Fanget, Véronique Ronat, Catherine Lesauder, Marie Laure Lavastre); Centre Hospitalier Général, Bastia, France (Alice Moulin*, Marie-France Turquini, Dominique Colombani, Danièle Belgodere); Centre Hospitalier Universitaire, Angers, France (Pascale Fialaire*, Stéphanie Proust, Sami Rehaiem); Centre Hospitalier Régional, Orléans, France (Louis Mesnard, Evelyne Werner*, Nathalie Dukiel, Baya Desmergers, Isabelle Blanc-Ruffat); APHP Hôpital Lariboisière, Paris, France (Barbara Maraux*, Anne Coursol, Julie Castaneda,Lise Etienne); CHR Arnaud de Villeneuve, Montpellier, France (Emmanuelle Vintejoux*, Muriel Lalande, Jacques Reynes, Michel Segondy, Nelly Guigue); Centre Hospitalier Général, Orsay, France (Christiane De Gennes*); Centre Hospitalier de Saint Martin, St Martin, France (Cyril Clavel*, François Cazassus, Véronique Walter); CHR Jeanne de Flandres, Lille , France (Françoise Mazingue*, Yamina Hammou, Marion Lagree, Odile Paquiez, Sophie D'angelo, Faiza Ajana, Laurence Boquet); Centre Hospitalier Dron, Tourcoing, France (Faïza Ajana); CHU - Maison de la Femme et de l'Enfant, Fort de France, France (Yves Hatchuel*, Imad Nahri, Jenny Zebelus); CHU Dupuytren, Limoges, France (Claire Genet*, Sophie Ducroix-Roubertou, Yves Aubrard, Anne Constanty, Pierre Weinbreck); Hôpital Intercommunal Sud Léman Valserine, Saint Julien, France (Emilie Piet*, Françoise Jacquier); Centre Hospitalier Saint Nazaire Cité Sanitaire, Saint Nazaire, France (Christophe Michaud*, Hassan Safwan, Arnaud Boutet, Carole Grand-Courault); Groupe Hospitalier Saint Joseph, Paris, France (Fanny Autret*, Fakher Habibi, Elie Azria); Centre Hospitalier Léon Binet, Provins, France (Mohamed Abdelhadi*); Centre Hositalier Andrée Rosemon, Cayenne, France (Narcisse Elenga*); Hôpital Calmette, Lille, France (Laurence Bocket, Françoise Taillet); Centre Hospitalier de Béziers, France (Gilles Palenzuela*, Redouane Khadly ,Danielle Pierronnet, Emmanuelle Dos-Santos); Centre Hospitalier de Narbonne (Selva David*); Hôpital Edouard Herriot, Lyon, France (Djamila Makhloufi*, Florence Brunel-Dalmas, Elisabeth Carbonnel-Delalande, Pierre Chiarello, Matthieu Godinot, Sylvie Gilbert); Hôpital Femme Mère Enfant, Bron, France (Jérôme Massardier*, Hélène Gauthier-Moulinier) ; Centre Hospitalier de la Basse-Terre, Guadeloupe (Elisabeth Fernandes*, Sata Ranaivojaona, Coralie Chevry)