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New Directions for IPF Treatment: Update on Clinical Trials

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Dr. Andrew Tager Symposium for Those Living with IPF
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Disclosures

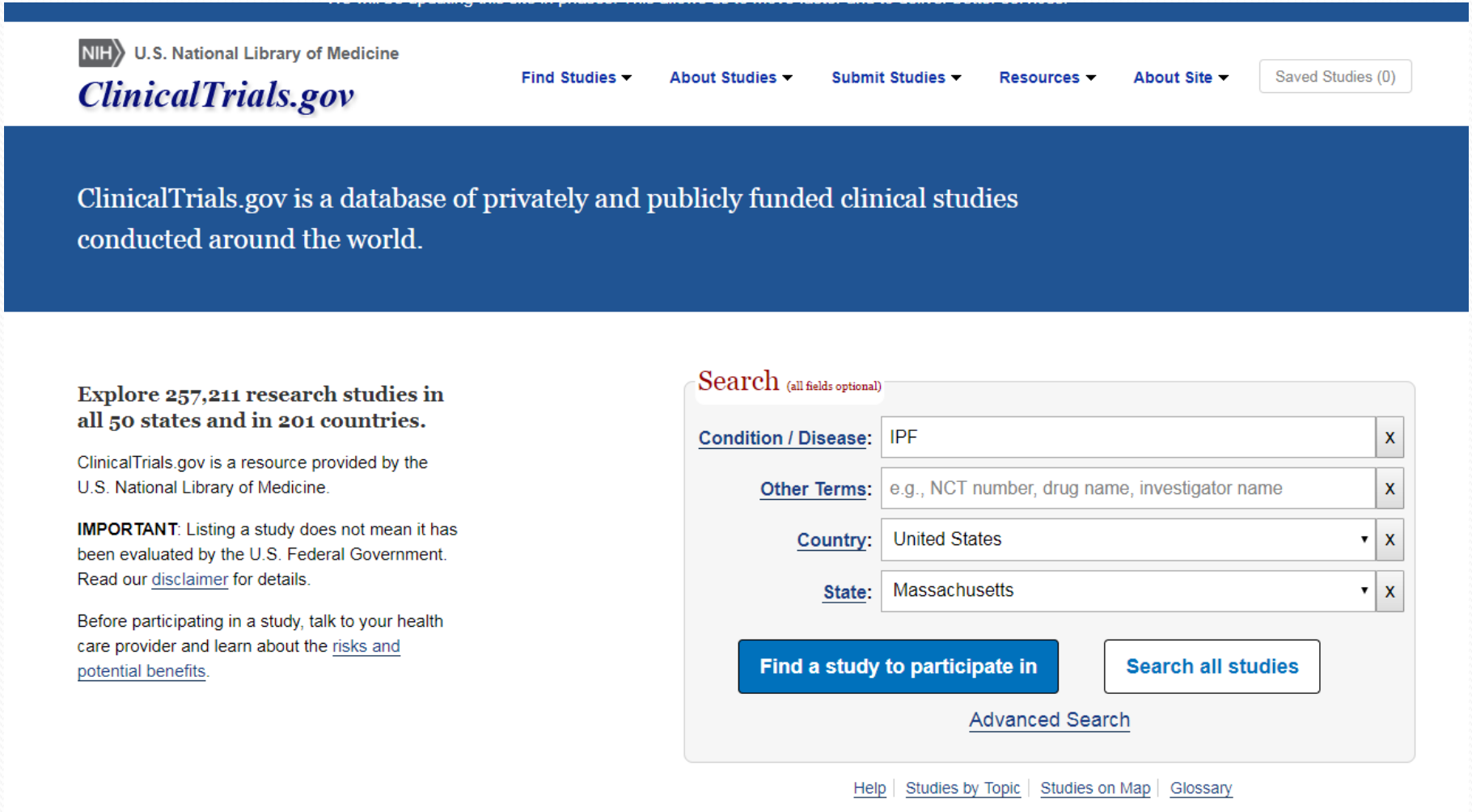
- Consulting for Boehringer Ingelheim (nintendanib) and Roche (pirfenidone and lebrikizumab)
- Site principal investigator for a Roche study (lebrikizumab)
- Advisory board for Boehringer Ingelheim (nintedanib)
- “Intellectual” bias/conflict of interest based on research interests/experience (BMS-986020, GLPG690, BG00011)

Has anyone participated in a clinical trial?

THANK YOU!

Clinical Trials

www.ClinicalTrials.gov



What are Clinical Trials?

- Research studies involving human volunteers (participants) intended to test new treatments (devices or drugs)
  - Unproven treatments – testing is for both effectiveness and safety
  - Treatment being tested may be compared to an available standard of care, to a placebo (inactive drug), or to nothing

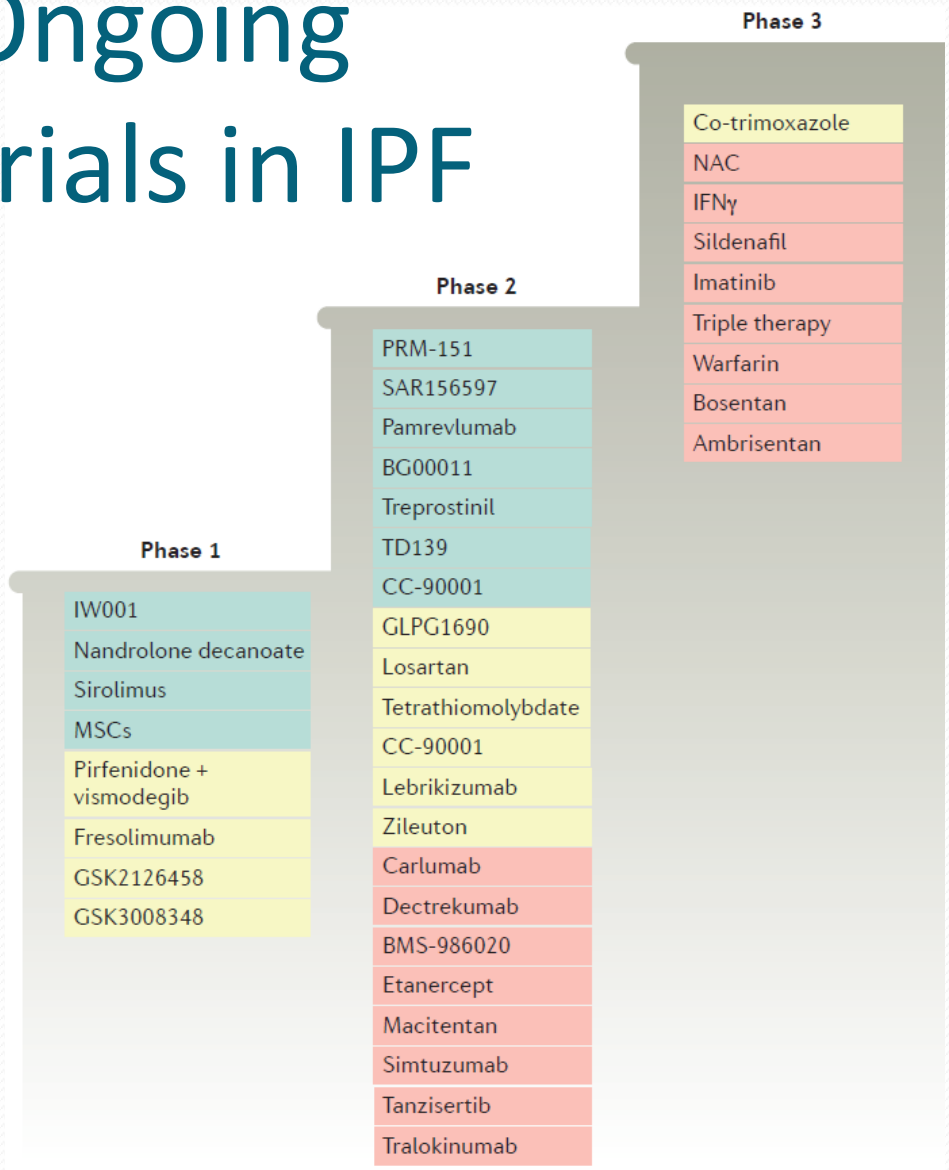
- Ultimate goal is to identify new treatments for a human illness that are both effective and safe

Clinical Trial Phases

Phase	Study Goals
I	• New drug, small number of participants (~10-50) • Assess safety/side effects, safe doses, and metabolism • Generally don't assess effectiveness

Often "placebo-controlled"

Recent/Ongoing Clinical Trials in IPF



From: Mora AL et al. Nat Rev Drug Discov. 2017.

Phase IV Studies: combination of pirfenidone + nintedanib

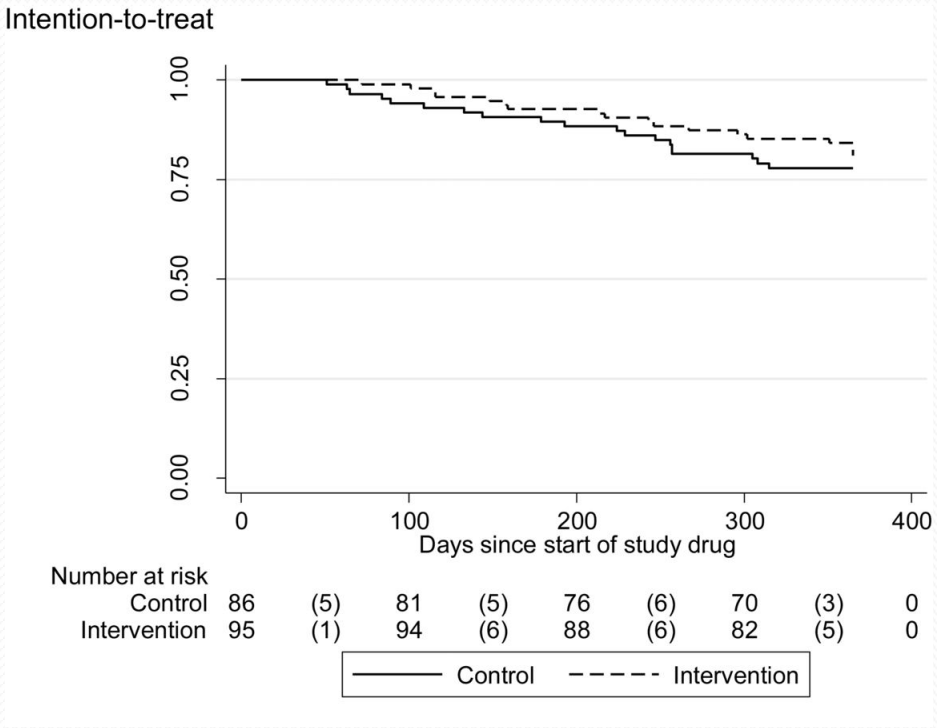
- INJOURNEY (Boehringer) – Phase IV study of nintedanib alone vs. nintedanib + pirfenidone (Vancheri C et al. *AJRCCM*. 2017)
  - 105 participants; 12 weeks duration
  - Similar rates of adverse events and treatment discontinuation in both groups; no difference in nintedanib metabolism
- Phase IV open-label study of pirfenidone + nintedanib (Roche)
  - 89 participants; 24 weeks
  - Combination therapy appeared to be safe (reported at ERS 9/2017)
- Larger studies examining efficacy of combination therapy expected in 2018

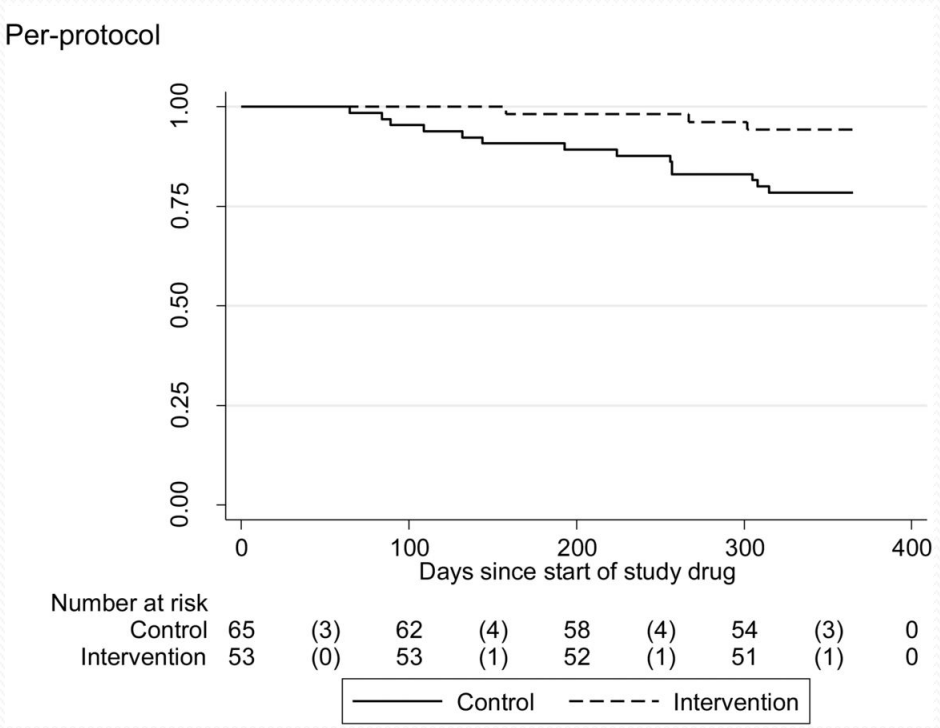
Phase III Studies: CleanUp IPF

- Phase III clinical trial of co-trimoxazole vs. placebo (added to standard care)
- NIH Sponsored / Pulmonary Trials Cooperative
- Target enrollment: 500 participants
- Duration: up to 42 months
- Currently enrolling – ClinicalTrials.gov identifier: NCT02759120

Existing data for co-trimoxazole in IPF

- Phase II study of co-trimoxazole vs. placebo for IPF (UK)
- 181 participants
- 12 months duration





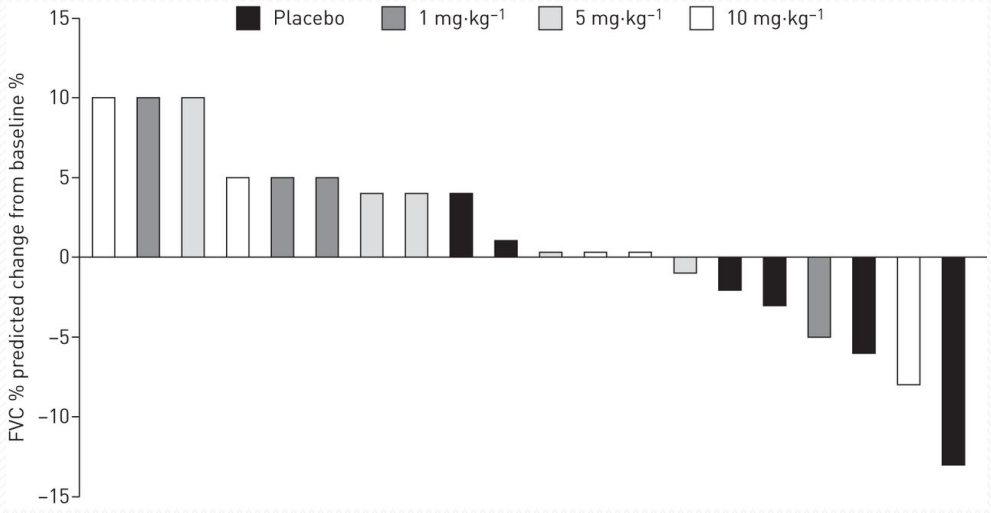
Shulgina L, et al. *Thorax*. 2013.

Phase III Studies – Sildenafil

- Phase III study of slidenafil vs. placebo added to nintedanib (Boehringer Ingelheim)
- Prior studies:
  - STEP-IPF (sildenafil vs. placebo) – No benefit overall but possible benefit in those with more severe disease
- Target enrollment: 250 participants (advanced disease)
- 24 week duration
- Currently enrolling – ClinicalTrials.gov identifier: NCT02802345

Phase II Studies - Pentraxin 2 (PRM-151) in IPF

- Recombinant human protein targeting immune system (Promedior)
- Phase I study of pentraxin-2 (5 doses) vs. placebo in IPF
  - 21 participants; up to 57 days duration
  - No serious adverse effects



Van der Blink B, et al. *ERJ*. 2016.

- Ongoing phase II study
  - Pentraxin 2 vs. placebo
  - 28 weeks
  - Completed enrollment (N = 117)
  - Results expected in 2018

Phase II Studies – Pamrevlumab (FG-3019) in IPF

- Humanized monoclonal antibody against CTGF (Fibrogen)
- Phase I/II study of FG-3019 (no placebo) in IPF
  - 89 participants; IV infusion every 3 weeks for 45 weeks
  - Safe and well-tolerated

Cohort	Subjects at BL n	FVC L		ΔFVC ⩽−10% predicted	ΔFVC >0% predicted
		Subjects n	ΔFVC L		
Cohort 1	53	38	−0.15	5 (13.2)	9 (23.7)
BL FVC ⩾55% predicted	38	33	−0.12	4 (12.1)	9 (27.3)
BL FVC <55% predicted	15	5	−0.37	1 (20.0)	0 (0.0)
Cohort 2	36	28	−0.13	4 (14.3)	10 (35.7)
BL FVC ⩾55% predicted	32	27	−0.11	3 (11.1)	10 (37.0)
BL FVC <55% predicted	4	1	−0.58	1 (100.0)	0 (0.0)
Cohort 1+2	89	66	−0.14	9 (13.6)	19 (28.8)
BL FVC ⩾55% predicted	70	60	−0.11	7 (11.7)	19 (31.7)
BL FVC <55% predicted	19	6	−0.40	2 (33.0)	0 (0.0)

- Ongoing phase II study
  - FG-3019 vs. placebo
  - 48 weeks
  - Completed enrollment (N = 160)
  - Results expected in 2018

Raghu G, et al. *ERJ*. 2016.

Phase II Studies – Lebrikizumab in IPF

- Humanized monoclonal antibody against interleukin-13 (Hoffman-La Roche)
- Safe and well-tolerated in multiple prior phase I and II studies in other diseases (asthma)
- Ongoing phase II study in IPF
  - Lebrikizumab vs. placebo (monotherapy or with pirfenidone)
  - 52 weeks
  - Completed enrollment (507)
  - Results expected 2018

Phase II Studies – BG00011 (STX-100) in IPF

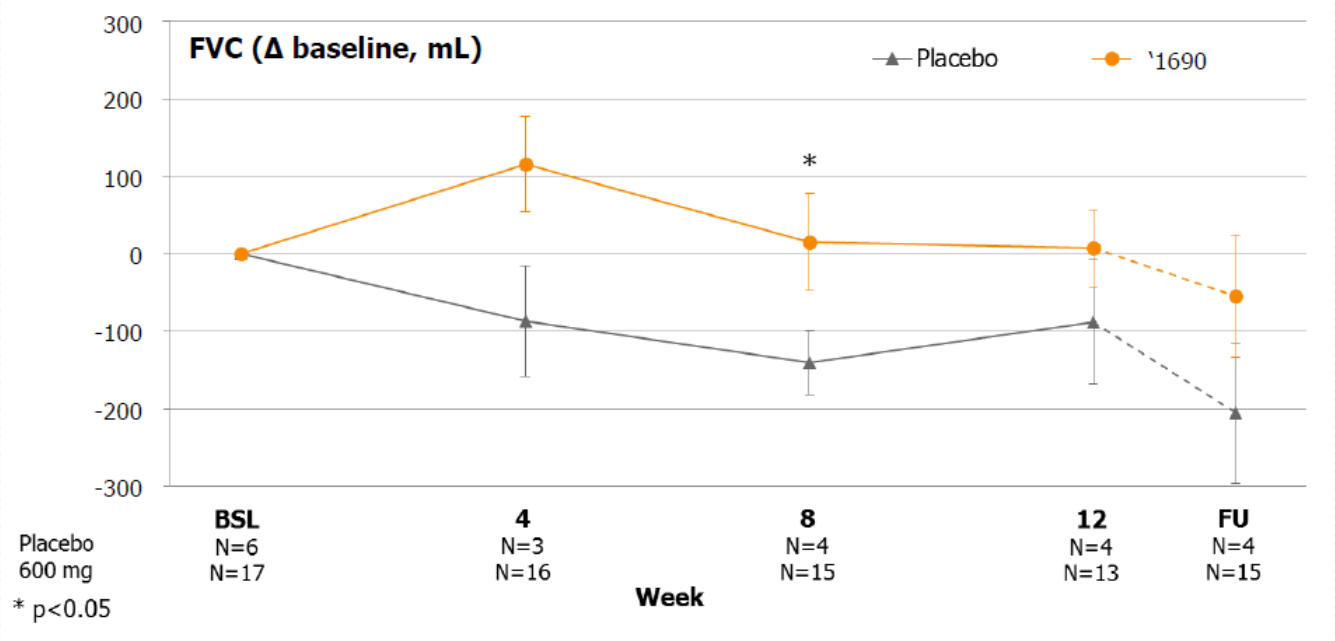
- Humanized monoclonal antibody against $\alpha_v\beta_6$ integrin (Biogen Idec)
- Phase II study of BG00011 vs. placebo
- 8 weeks duration
- Completed enrollment (43)
- Results expected 2018

Phase II Studies - BMS-986020 in IPF

- Inhibitor of lysophosphatidic acid (LPA) receptor-1 (Bristol-Myers Squibb)
- Phase II study of BMS-986020 vs. placebo in IPF
- 80 participants; 26 weeks
- Completed; awaiting results

Phase I Studies – GLPG1690 in IPF

- Inhibitor of autotaxin (ATX); Galapagos
- Phase I study of GLPG1690 vs. placebo in IPF
- 23 participants; 12 weeks
- Results not yet published



DISCLAIMER – Results from Galapagos website!

Phase I Studies – Stem Cell Therapy in IPF

- Mesenchymal stem cells (MSCs) may promote repair (regeneration?) of injured/fibrotic lung
- Phase I study of MSCs in IPF (Australia; Chambers et al. 2014)
  - 8 participants (2 doses)
  - No serious adverse events; minor, transient drop in oxygen levels
  - No change in lung function at 6 months
- Phase I study of MSCs in IPF (USA; Glassberg et al. 2017)
  - 9 participants (3 doses)
  - No immediate reactions or treatment-related adverse effects
  - Followed for 60 weeks
  - 2 deaths – both in the highest dose group; most severe disease at baseline

Summary

- Many ongoing/recently completed IPF clinical trials with expected results in the near future
- Numerous enrolling/upcoming clinical trials for IPF
  - 8 drug trials actively enrolling in the U.S. according to ClinicalTrials.gov (Phase I → III)
  - More trials expected in 2018
- Resources:
  - www.ClinicalTrials.gov
  - ILD Collaborative Website: http://www.ildcollaborative.org/clinical-trials
- To all those who have participated in clinical research……

THANK YOU!!!!!!