

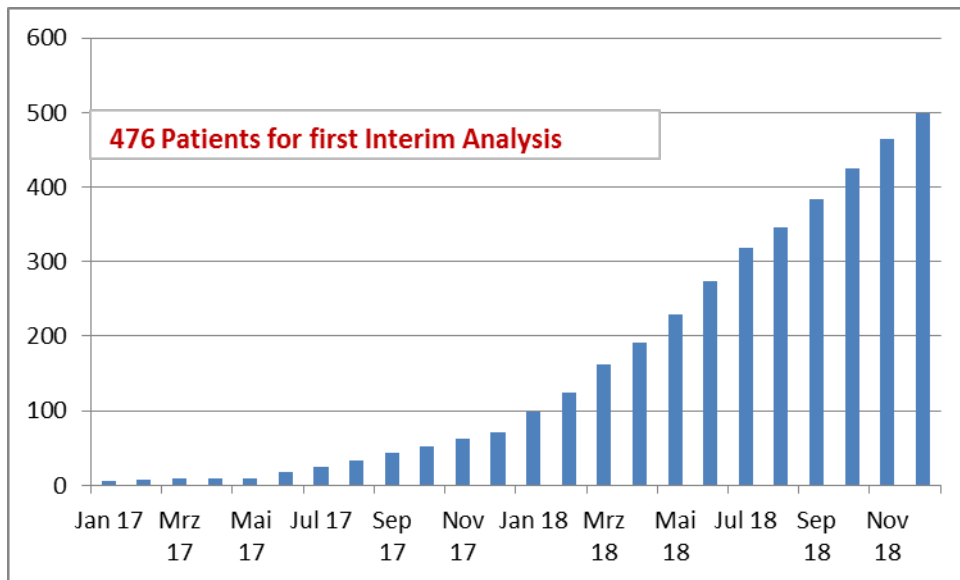
PROTHOR Newsletter 4/2018

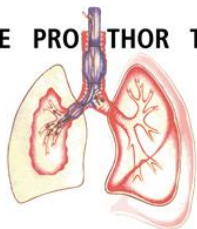
Dresden, December 30, 2018

Dear National Coordinators and Local Investigators of PROTHOR,

The year 2018 will end in a few days and we would like to take this opportunity to thank you for your contribution to the PROTHOR project. In January 2017 the center of Istanbul and Dresden started the study with the inclusion of the first patients. Several centers joined the study in the following months, and we reached 71 randomized patients in December 2017. One year later, we have reached the magic number of 500 patients in December 2018. Thank you so much for your effort and congratulations to all contributors!

Overview of randomized patients over time



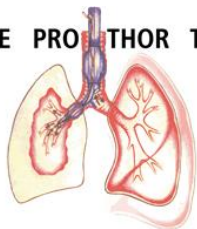


Completeness of datasets & Interim analysis

We have passed the first interim analysis point (476 patients, 20% of total sample size). We kindly ask you to complete all existing records by January 31. We will check your entries and give you feedback. Once the data has been checked, we will then analyze and present the results to the DSMB. All centers can continue with patient recruitment, but completeness of existing data has high priority. The following table gives an overview of the centers and the corresponding patient “cutoff” numbers. Please complete all existing patient records of your center up to the “cutoff” patient number!

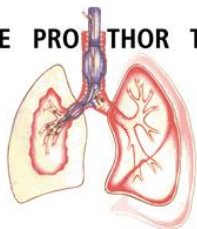
Overview of the randomized patients per center

Center number	Center name	Patient number cutoff
001	Istanbul	001032
002	Dresden	002026
003	Magdeburg	003004
004	Coswig	004050
005	Münster	zero
006	NYC Cornell Medical College	006010
007	LMU München	007020
008	Hospital General Universitario de Valencia	008002
009	Freiburg	009035
010	Insular Hospital Gran Canaria	010007
011	Amsterdam	011011
012	Aachen	012003



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013	Hospital Vigo, Spain	012027
014	Zagreb	014026
015	Sotiria, Greece	015042
016	Bucharest	zero
017	Belgrade	017025
018	La Ribera, Spain	018029
019	Genova	019013
020	Prague	020001
021	Barcelona, Spain	021016
022	Bucharest	zero
023	Radboud	023030
024	Attikon	024024
025	Ljubljana	025016
026	Foggia	026023
027	Lannelongue, France	zero
028	Merheim, Germany	zero
029	Heraklion	029019
030	Fudan, China	030018
031	Ferrara, Italy	031010
032	Nis, Serbia	032001
033	Taichung, Taiwan	zero
034	Messina, Italy	034001
035	Rijnstate	035001



Support from ESA and EACTA

Our study is endorsed by ESA. Due to the effort of our steering committee, our trial was visible for a time period of 1 week on the main page of ESA's clinical trial network website. This drew the attention to our study and subsequently several centers joined the study. In autumn 2018, EACTA endorsed our study and mentioned our study in their regular newsletter which also provided contact to new centers.

Publication of the study protocol in TRIALS

The manuscript of the PROTHOR STUDY PROTOCOL has been sent to TRIALS (trialsjournal.com). Three reviewers have given their feedback. We will prepare the revised manuscript within a narrow timeframe.

Happy new year & best regards,

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