Survival and Benefit of Upfront Combination Therapy: Registry of Japanese Patients with Pulmonary Arterial Hypertension ～ Data from Japan PH Registry (JAPHR) ～

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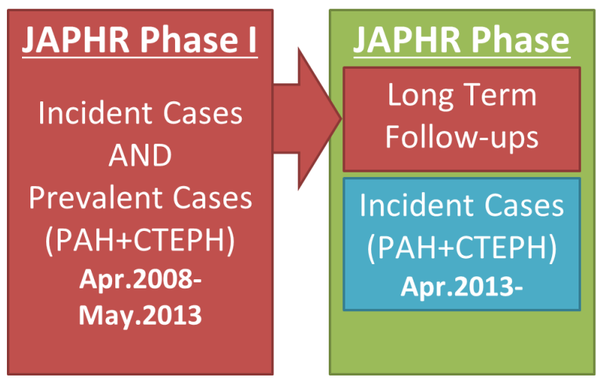
Background

Many countries have their own national registries for PH to investigate real-world data for in PH treatment. However, there was no national registry for PH in Japan for long time. So we establish a nation-wide PH registry under the government support.

Design

Japan PH Registry (JAPHR): Phase I



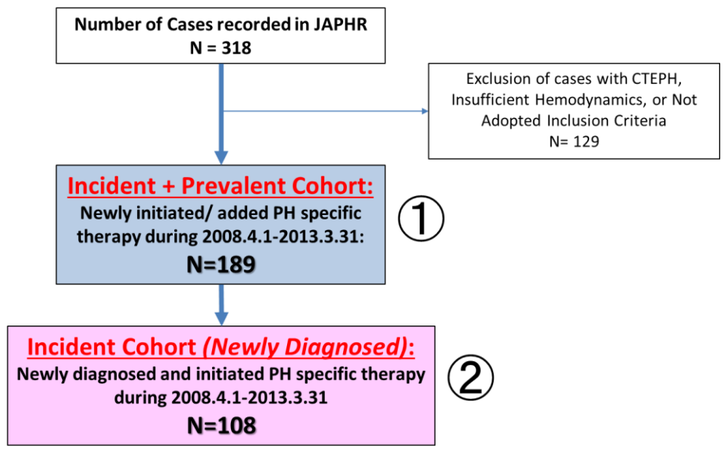
Inclusion Criteria :

- Newly initiated/added PH specific therapy in each centers
- Diagnosed as PAH/CTEPH (Dana point 1, 4, (5))
- Age > 18 years old and provided written informed consent

Activated Centers (JAPHR Phase I)

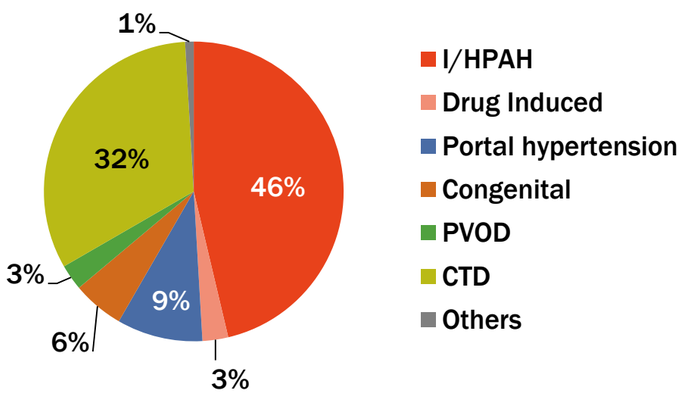
- Chiba University
- Hokkaido University
- Keio University
- Kyorin University
- Kyushu University
- Nara Medical University
- Okayama Medical Center
- University of Tokyo

Study Cohort

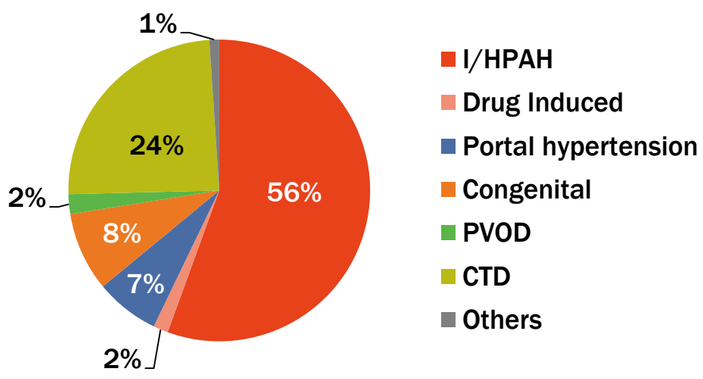


Patients Characteristics: Etiology

Incident Cases N=108



All Cases (Incident + Prevalent) N=189



Baseline Characteristics at Entry

Incident Cases N=108

	Incident Cases (N=108)	I/HPAH + Drug (N=50)
Age (y.o.) ± SD	48.8 ± 17.3	42.0 ± 14.8
Female, N (%)	86 (79.6%)	37 (74.0%)
6MWD (m) ± SD	281 ± 145 (m)	326 ± 143 (m)
NYHA		
I , N (%)	1 (0.9%)	1 (2.0%)
II, N (%)	36 (33.3%)	17 (34.0%)
III, N (%)	55 (50.9%)	24 (48.0%)
IV, N (%)	16 (14.8%)	8 (16.0%)
Rhythm		
Sinus, N (%)	105 (97.2%)	71 (98.6%)
Afib, N (%)	2 (1.9%)	1 (2.7%)
Others, N (%)	1 (0.9%)	0 (0%)
Use of Anticoagulant, N (%)	46 (42.6%)	34 (46.6%)

	Incident Cases (N=108)	I/HPAH + Drug (N=50)
Hemodynamics		
SvO_2 (%)	65.0 ± 8.9	65.5 ± 9.3
mean PA pressure (mmHg)	46.9 ± 14.4	52.2 ± 14.5
PVR (dyne·sec/cm^5)	1106 ± 733	1223 ± 801
PA wedge pressure (mmHg)	7.8 ± 3.7	8.6 ± 3.9
RA pressure (mmHg)	6.5 ± 4.0	7.2 ± 4.5
Cardiac Index (L/min/m^2)	2.2 ± 0.7	2.2 ± 0.8

All Cases (Incident + Prevalent) N=189

	All Cases (N=189)	I/HPAH + Drug (N=108)
Age (y.o.) ± SD	45.1 ± 16.6	40.0 ± 13.9
Age at Diagnosis (y.o.) ± SD	43.9 ± 16.9	39.5 ± 14.3
Female, N (%)	144 (76.2%)	79 (73.1%)
6MWD (m) ± SD	306 ± 146 (m)	343 ± 138 (m)
NYHA		
I , N (%)	4 (2,1%)	3 (2.8%)
II, N (%)	64 (33.9%)	40 (37.0%)
III, N (%)	96 (50.8%)	52 (48.1%)
IV, N (%)	25 (13.2%)	13 (12.0%)
Rhythm		
Sinus, N (%)	183 (96.8%)	107 (99.1%)
Afib, N (%)	4 (2.1%)	1 (0.9%)
Others, N (%)	2 (1.1%)	0 (0%)
Use of Anticoagulant, N (%)	78 (41.3%)	47 (43.5%)

	All Cases (N=189)	I/HPAH + Drug (N=108)
Hemodynamics		
SvO_2 (%)	66.6 ± 9.7	66.8 ± 9.0
mean PA pressure (mmHg)	48.2 ± 13.8	50.2 ± 13.3
PVR (dyne·sec/cm^5)	1036 ± 653	1085 ± 728
PA wedge pressure (mmHg)	8.3 ± 3.4	8.7 ± 3.4
RA pressure (mmHg)	6.6 ± 4.1	6.8 ± 4.3
Cardiac Index (L/min/m^2)	2.4 ± 0.8	2.4 ± 0.9

Results

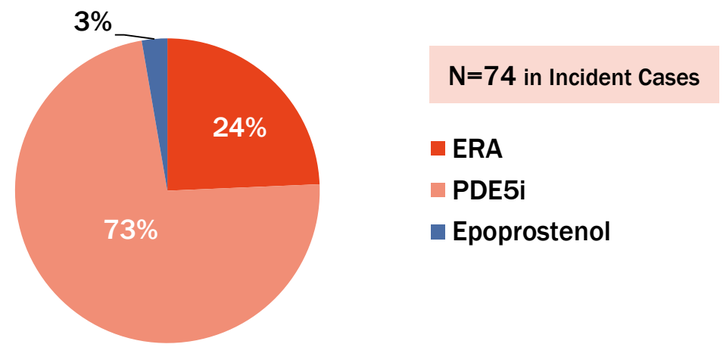
Initial Drug Combinations for the incident cohort

	Drug Combination	N	%
Single	Sildenafil	38	36.2
	Tadalafil	16	14.8
	Bosentan	14	13.0
	Ambrisentan	4	3.7
	Epoprostenol	2	1.9
Upfront-Dual	Bosentan + sildenafil	7	6.5
	Ambrisentan + sildenafil	7	6.5
	Bosentan + epoprostenol	5	4.6
	Sildenafil + epoprostenol	5	4.6
	Bosentan + tadalafil	4	3.7
	Ambrisentan + tadalafil	2	1.9
	Tadalafil + epoprostenol	1	0.9
Upfront-Triple	Bosentan +sildenafil +epoprostenol	2	1.9
	Ambrisentan +tadafil +epoprostenol	1	0.9
Total		108	100

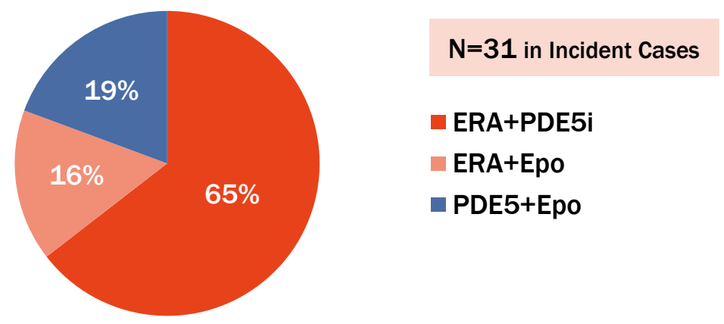
Initiation of two or more drugs within 90 days are considered concurrent.

Drug Administration at Entry

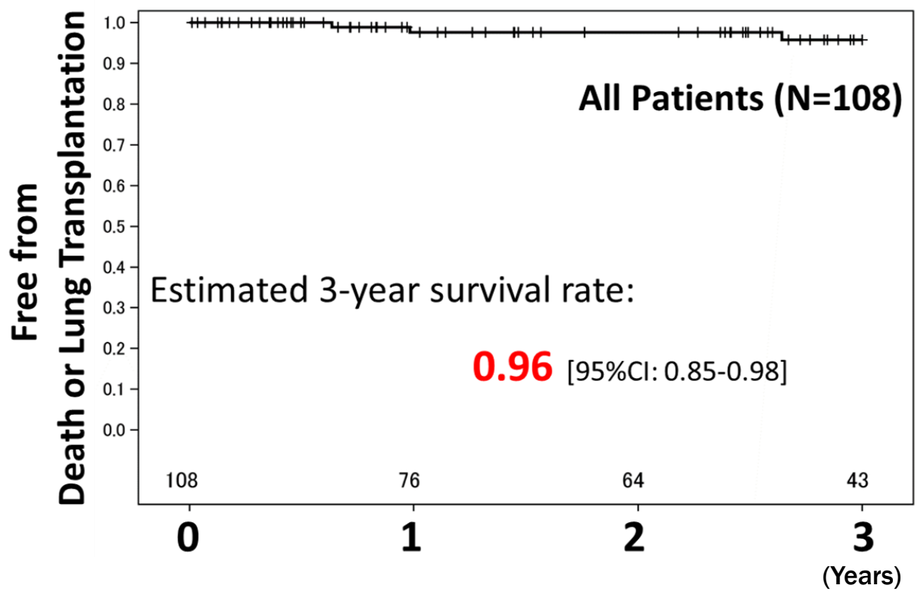
Single Therapy



Upfront Double Combination Therapy



5-year Survival Analysis for Patients in the Incident Cohort



Summary

Survival Data

- 3-year survival rate is **96%** (N=108) in the incident cohort.

Unique Points in Japan

- In the incident cohort, **32%** cases had already received **upfront combination therapies**.

Declaration of interest: This study was supported by Actelion Pharmaceuticals Japan.