Clinical Trial Emulation of the CATT Using Data from the IRIS® Registry

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Purpose

- To emulate the prn arms of the Comparison of Age-Related Macular Degeneration Treatment Trials (CATT) using real world data (RWD) from the IRIS Registry
- To compare the baseline characteristics and clinical outcomes of the RWD arms to the clinical trial arms for monthly ranibizumab and bevacizumab treatment

Methods

- All non-imaging based criteria from the CATT that could be ascertained from RWD were applied to IRIS Registry patients from Jan 1, 2015 to Dec 31, 2019
- All eyes evaluated every four to six weeks and injected prn with either bevacizumab or ranibizumab only for one year were included
- Baseline demographic and clinical characteristics, as well as clinical outcomes from the CATT were evaluated for the bevacizumab and ranibizumab RWD cohorts

Results

- The IRIS Registry contained 531,133 patients with nAMD receiving bevacizumab or ranibizumab
- After applying the inclusion and exclusion criteria, as well as treatment requirements, the real-world prn cohort included 427 study eyes treated with ranibizumab and 771 study eyes treated with bevacizumab
- Baseline clinical and demographic information (Table 1) as well as clinical outcomes (Table 2) are described below
- Compared to the monthly treatment trial arms, the RWD arms had similar baseline demographic and clinical characteristics
- On average, the RWD prn arms received 8.98 ranibizumab injections and 7.65 bevacizumab injections in one year compared to 11.7 and 11.9, respectively, in the trial arms

Conclusion

- The findings in this study suggest that clinical trial populations are not representative of patients in the real-world and highlight the potential insight RWD can provide on a broader patient population
- Real world treatment patterns for nAMD typically result in significantly fewer injections in the first year of treatment and decreased visual acuity gains compared to clinical trial populations, particularly when patients are treated monthly in clinical trial protocols
- This proof-of-concept study demonstrates how RWD can be used to emulate clinical trial arms

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IRIS Registry Data	CATT Trial Data	Outcomes
Cohort 1: Treatment-naïve nAMD patients treated with bevacizumab only for 1 year on a prn basis	**Cohort 3:** Treatment-naïve nAMD patients treated with bevacizumab only for 1 year on a monthly basis	**Primary Outcome:** Mean Change in visual acuity (ETDRS letters) between baseline and 1 year
Cohort 2: Treatment-naïve nAMD patients treated with ranibizumab only for 1 year on a prn basis	**Cohort 4:** Treatment-naïve nAMD patients treated with ranibizumab only for 1 year on a monthly basis	**Secondary Outcomes:** • Proportion of patients with a change in visual acuity of 15 letters or more • Number of injections at 1 year • Annual drug cost (assuming $2,000/dose for ranibizumab and $50/dose for bevacizumab) • Incidence of ocular adverse events (endophthalmitis)

Table 1: Baseline Demographic and Clinical Characteristics

	CATT Trial Data				IRIS Overall Real-World Cohorts			
	Ranibizumab monthly (N = 301)		Bevacizumab monthly (N = 286)		Ranibizumab as needed (N=427)		Bevacizumab as needed (N=771)	
Characteristic	**N (or mean)**	**% (or SD)**	**N (or mean)**	**% (or SD)**	**N (or mean)**	**% (or SD)**	**N (or mean)**	**% (or SD)**
Age								
50-59 yr	2	0.7%	1	0.3	1	0.2%	11	1.4%
60-69 yr	33	11.0%	28	9.8	30	7.0%	58	7.5%
70-79 yr	102	33.9%	84	29.4	139	32.6%	231	30.0%
80-89 yr	142	47.2%	150	52.4	198	46.4%	362	47.0%
>= 90 yr	22	7.3%	23	8.0	59	13.8%	109	14.1%
Mean (yr), SD	79.2	7.2	79.9	7.0	81.16	7.5	81.1	8.0
Sex, n (%)								
Female	183	60.8%	180	62.9%	293	68.6%	474	61.5%
Male	118	39.2%	106	37.1%	132	30.9%	293	38.0%
Race, n (%)								
White or Caucasian	297	98.7%	281	98.3%	388	90.9%	696	90.3%
Other	4	1.3%	5	1.7%	10	2.3%	25	3.2%
Unknown					29	6.8%	50	6.5%
Visual-acuity score and Snellen equivalent								
68-82 letters, 20/25 - 20/40	111	36.9%	94	32.9%	150	35.1%	265	34.4%
53-67 letters, 20/50 - 20/80	98	32.6%	118	41.3%	178	41.7%	318	41.3%
38-52 letters, 20/100 - 20/160	67	22.3%	53	18.5%	44	10.3%	108	14.0%
23-37 letters, 20/200 - 20/320	25	8.3%	21	7.3%	55	12.9%	80	10.4%
Mean number of letters	60.1	14.3	60.2	13.1	60.3	13.2	60.2	12.5

Table 2: Clinical Outcomes at One Year for CATT Monthly and IRIS Registry prn Cohorts

	CATT Trial Data				IRIS Overall Real-World Cohorts			
	Ranibizumab monthly (N = 301)		Bevacizumab monthly (N = 286)		Ranibizumab as needed (N=427)		Bevacizumab as needed (N=771)	
Outcome	**N (or mean)**	**% (or SD)**	**N (or mean)**	**% (or SD)**	**N (or mean)**	**% (or SD)**	**N (or mean)**	**% (or SD)**
Visual-acuity score and Snellen equivalent								
83-97 letters, 20/12 - 20/20	42	14.8%	45	17.0%	6	1.4%	21	2.7%
68-82 letters, 20/25 - 20/40	149	52.5%	134	50.6%	179	41.9%	308	40.0%
53-67 letters, 20/50 - 20/80	52	18.3%	47	17.7%	135	31.6%	230	29.8%
38-52 letters, 20/100 - 20/160	23	8.1%	21	7.9%	33	7.7%	52	6.7%
<=37 letters, <= 20/200	17	6.3%	18	6.8%	37	8.7%	86	11.2%
Mean number of letters	68.9	17.6	68.4	18.2	62.9	15.7	62.15	17.6
Change from baseline visual-acuity score								
Increase of >= 15 letters	97	34.2%	83	31.3%	73	18.7%	130	18.7%
Increase of 5-14 letters	90	31.7%	98	37.0%	97	24.9%	175	25.1%
Change of <=4 letters	62	21.8%	50	18.9%	117	30.0%	204	29.3%
Decrease of 5-14 letters	19	6.7%	18	6.8%	61	15.6%	106	15.2%
Decrease of >= 15 letters	15	5.6%	16	6.0%	42	10.8%	82	11.8%
Mean number of letters	8.6	13.9	8.0	15.8	2.5	14.8	2.0	15.9
Treatments								
Mean number of injections (+/- SD)	12.4	1.6	12.6	1.3	9.0	3.4	7.7	3.6
Average treatment frequency (weeks)	4.5	0.5	4.4	0.4	6.3	4.0	7.2	5.4
Cost Analysis								
Average cost of drug/patient ($)	$24,742		$631		$17,953.16	$6,699.29	$382.68	$7,154.16