

Intravitreal therapies and their patterns of use in Lombardy Region

Emanuela Foglia^{1,2}, Federica Asperti^{1,2}, Daniele Bellavia^{1,2}, Fabrizio Schettini^{1,2}, Elisabetta Garagiola^{1,2}, Andrea Macchiavelli³, Diego Merlo³, Giovanna Mainardi⁴, Paolo Lusuriello⁴, Michela Franzin⁵, Nicola Soliveri⁵, Raffaella Lombardo⁶, Lucia Ventura⁶, Gabriella Pieri⁷, Corrado Punzi⁷, Maria Fazio⁸, Ciro Di Carlo⁸, Lucrezia Ferrario^{1,2}

¹ Carlo Cattaneo – LIUC University and LIUC Business School, Castellanza, Italy; ² HD LAB – Healthcare Datasience LAB - Carlo Cattaneo – LIUC University, Castellanza, Italy; ³ Pharmaceutical Department, ASST Cremona, Cremona, Italy; ⁴ Pharmaceutical Department, ASST Valle Olona, Busto Arsizio, Italy; ⁵ Pharmaceutical Department, ASST Papa Giovanni XXIII, Bergamo, Italy; ⁶ Pharmaceutical Department, ASST Santi Paolo e Carlo, Milano, Italy; ⁷ Pharmaceutical Department, IRCCS Humanitas, Milano, Italy; ⁸ Pharmaceutical Department, San Raffaele Research Institute, Milano, Italy

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Rationale of the study

- **Anti-VEGF and sustained-release corticosteroids implants have revolutionized the care of wet age-related macular degeneration (AMD), retinal vein occlusion (RVO), diabetic macular edema (DME) and choroidal neovascularization (CNV)**
- Several multi-centre randomised trials have demonstrated the efficacy of all the licensed drugs available in the clinical practice for the treatment of such sight-threatening diseases: monthly dosing with ranibizumab and aflibercept was recommended (considering a range between 7 and 12 intravitreal injections), whereas corticosteroids required at least 2.3 injections, within the first year of treatment after diagnosis

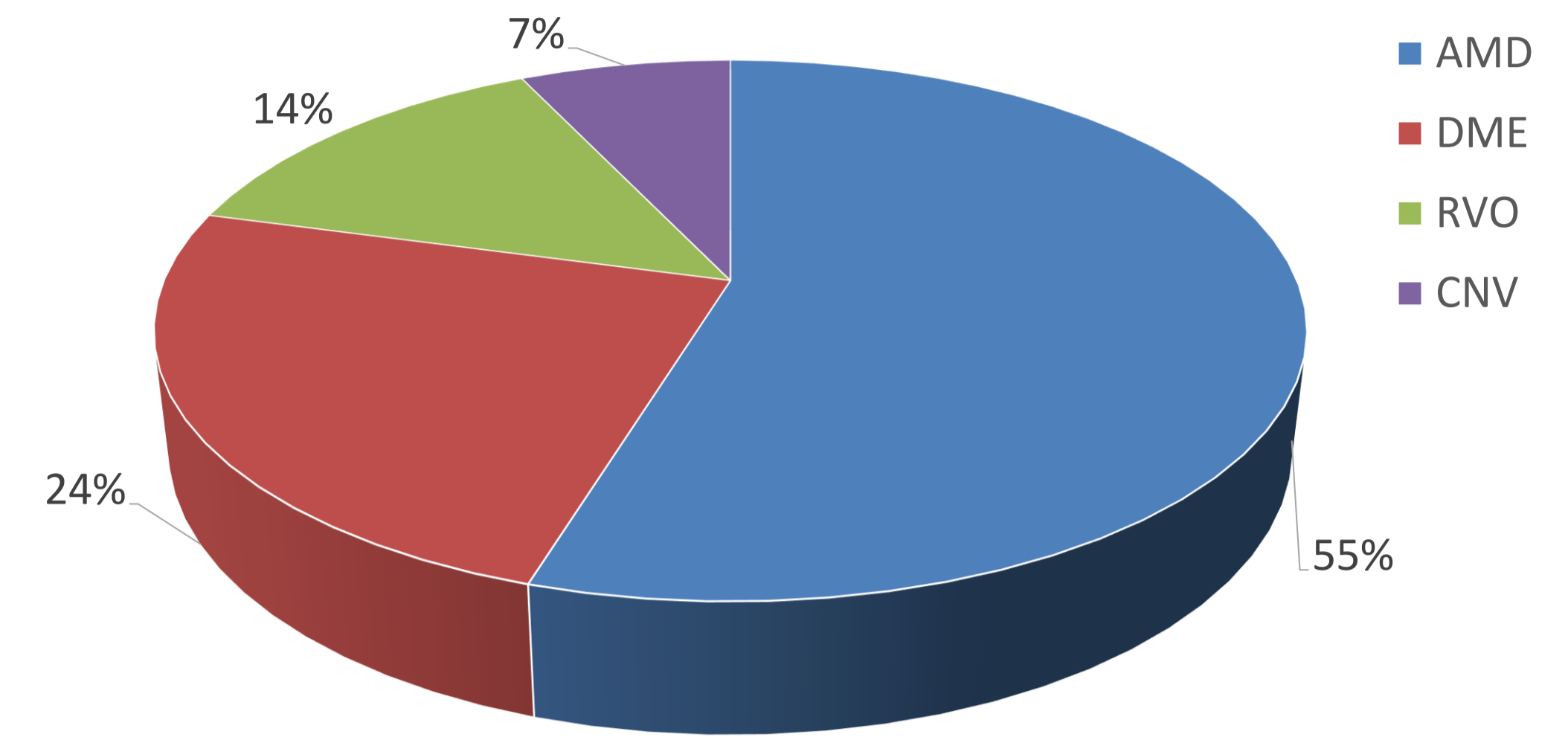
Objectives and Methods

To investigate drugs' utilization and prescribing practices concerning wet age-related macular degeneration (wAMD), retinal vein occlusion (RVO), diabetic macular edema (DME) and choroidal neovascularization (CNV) licensed intravitreal therapies, providing Lombardy Region real-world evidence

- In 2022-2023, a **retrospective observational multi-center study**, based on anonymous data from pharmacy databases, was conducted in **8 Italian hospitals**
- Treatment-naïve wAMD, RVO, DME, and CNV eyes, receiving an intravitreal injection from **06/01/2019 to 12/31/2020**, were included and a 24-month time horizon was assumed
- **The typology of administered drugs and number of intravitreal injections were collected**

The sample under assessment

- 3,858 eyes were diagnosed for a maculopathy
- 53% received treatment up to 24 months



Patients' Follow-up	N.	%
Two-year treatment, without any therapeutical switch	976	25.30%
One-year treatment, without any therapeutical switch	1,570	40.70%
One-year treatment, with a therapeutical switch	250	6.50%
One-year treatment, with two therapeutical switches	10	0.30%
Two-year treatment, with a therapeutical switch occurring within the first year	824	21.40%
Two-year treatment, with a therapeutical switch occurring within the second year	105	2.70%
Two-year treatment, with a therapeutical switch occurring within the first and the second year	123	3.20%
Total	3,858	100%

Results

Average number of injections delivered to eyes treated only during the first year after diagnosis, without any experiences of therapeutical switch

Maculopathy	Intravitreal drug	Number of intravitreal injections	Suggested Therapeutic Scheme (12 months)
AMD (723 eyes)	AFLIBERCEPT	2.99 ± 0.087 [range: 1-9]	12.1 (Heier <i>et al.</i> , 2012)
	BEVACIZUMAB	3.39 ± 0.106 [range: 1-10]	8.7 (Amarakoon <i>et al.</i> , 2018)
	RANIBIZUMAB	2.94 ± 0.117 [range: 1-9]	12 (Rosenfeld <i>et al.</i> , 2006)
DME (409 eyes)	AFLIBERCEPT	3.69 ± 0.192 [range: 1-10]	8.5 (Korolbelnik <i>et al.</i> , 2014)
	BEVACIZUMAB	2.75 ± 0.222 [range: 1-8]	9.7 (Wells <i>et al.</i> , 2015)
	DEXAMETHASONE	1.67 ± 0.062 [range: 1-4]	2.3 (Boyer <i>et al.</i> , 2014)
	RANIBIZUMAB	3.49 ± 0.275 [range: 1-13]	7 (Mitchell <i>et al.</i> , 2011)
	FLUOCINOLONE	1	N/A
RVO (277 eyes)	TRIAMCINOLONE	1	2,1 (Neto <i>et al.</i> , 2017) [6-month time horizon]
	AFLIBERCEPT	3.32 ± 0.147 [range: 1-8]	8,7 (Heier <i>et al.</i> , 2014)
	DEXAMETHASONE	1.43 ± 0.055 [range: 1-3]	3.2 (Haller <i>et al.</i> , 2010) [6-month time horizon]
CNV (165 eyes)	RANIBIZUMAB	3.31 ± 0.244 [range: 1-9]	8,8 (Tadayoni <i>et al.</i> , 2016)
	RANIBIZUMAB	2.85 ± 0.266 [range: 1-9]	3.5 – 4.6 (Wolf <i>et al.</i> , 2014)
	AFLIBERCEPT	2.37 ± 0.124 [range: 1-9]	3 (Ikuno <i>et al.</i> , 2015)

Average number of injections delivered to eyes treated only during the first year after diagnosis, with an experience of therapeutical switch

AMD	Number of intravitreal injections (First drug)	Number of intravitreal injections (Second drug)
AFLIBERCEPT+BEVACIZUMAB	2.68	2.07
RANIBIZUMAB+BEVACIZUMAB	2.89	2.2
BEVACIZUMAB+RANIBIZUMAB	2.13	2.31
BEVACIZUMAB+AFLIBERCEPT	4.95	3.27
AFLIBERCEPT+RANIBIZUMAB	3.22	2.11
RANIBIZUMAB+AFLIBERCEPT	3.11	3.33
DME	Number of intravitreal injections (First drug)	Number of intravitreal injections (Second drug)
AFLIBERCEPT+DEXAMETHASONE	3.57	1.79
RANIBIZUMAB+AFLIBERCEPT	2.87	2.63
AFLIBERCEPT+BEVACIZUMAB	2.71	3
RANIBIZUMAB+BEVACIZUMAB	3.8	3
RANIBIZUMAB+DEXAMETHASONE	5.6	1.2
AFLIBERCEPT+RANIBIZUMAB	3.25	2.25
DEXAMETHASONE+RANIBIZUMAB	1.75	3.25
DEXAMETHASONE+AFLIBERCEPT	1.25	2.75
DEXAMETHASONE+BEVACIZUMAB	1.33	1.67
BEVACIZUMAB+RANIBIZUMAB	2.67	2
BEVACIZUMAB+DEXAMETHASONE	3	1
TRIAMCINOLONE+DEXAMETHASONE	1	1
DEXAMETHASONE+FLUOCINOLONE	2	2
RVO	Number of intravitreal injections (First drug)	Number of intravitreal injections (Second drug)
AFLIBERCEPT+DEXAMETHASONE	2.88	1.38
RANIBIZUMAB+DEXAMETHASONE	2.5	1.67
RANIBIZUMAB+AFLIBERCEPT	2,33	4.33
AFLIBERCEPT+BEVACIZUMAB	2.67	1.33
DEXAMETHASONE+AFLIBERCEPT	1	3
DEXAMETHASONE+RANIBIZUMAB	1	1
CNV	Number of intravitreal injections (First drug)	Number of intravitreal injections (Second drug)
RANIBIZUMAB+AFLIBERCEPT	1.75	2.5

Average number of injections delivered to eyes treated for two years after diagnosis, without any experiences of therapeutical switch

Maculopathy	Intravitreal drug	Number of intravitreal injections (I year)	Number of intravitreal injections (II year)	Cumulative number of intravitreal injections (24 months)	Suggested Therapeutic Scheme (24 months)
AMD (455 eyes)	AFLIBERCEPT	4.67 ± 0.201	3.73 ± 0.183	8.39 ± 0.324	16.8 (Schmidt-Erfurth <i>et al.</i> , 2014)
	BEVACIZUMAB	4.57 ± 0.149	3.69 ± 0.120	8.26 ± 0.221	8.7 (Amarakoon <i>et al.</i> , 2018) [12-month time horizon]
	RANIBIZUMAB	4.78 ± 0.241	3.62 ± 0.221	8.4 ± 0.386	24 (Rosenfeld <i>et al.</i> , 2006)
DME (268 eyes)	AFLIBERCEPT	4.81 ± 0.220	3.11 ± 0.172	7.91 ± 0.325	13.5 (Korolbelnik <i>et al.</i> , 2014)
	BEVACIZUMAB	3.53 ± 0.421	2.65 ± 0.402	6.18 ± 0.589	9.7 (Wells <i>et al.</i> , 2015) [12-month time horizon]
	DEXAMETHASONE	2.46 ± 0.106	2 ± 0.108	4.46 ± 0.184	3.3 (Boyer <i>et al.</i> , 2014)
RVO (172 eyes)	RANIBIZUMAB	4.28 ± 0.316	2.66 ± 0.246	6.94 ± 0.482	10.9 (Mitchell <i>et al.</i> , 2011)
	AFLIBERCEPT	4.2 ± 0.219	3.26 ± 0.184	7.45 ± 0.335	12 (Heier <i>et al.</i> , 2014)
	DEXAMETHASONE	1.88 ± 0.120	1.56 ± 0.090	3.44 ± 0.150	3.2 (Haller <i>et al.</i> , 2010) [6-month time horizon]
CNV (90 eyes)	RANIBIZUMAB	5.12 ± 0.410	3.79 ± 0.376	8.91 ± 0.701	16.8 (Tadayoni <i>et al.</i> , 2016)
	AFLIBERCEPT	4.8 ± 0.694	3.45 ± 0.545	8.25 ± 1.117	3 (Ikuno <i>et al.</i> , 2015) [12-month time horizon]
	RANIBIZUMAB	3.57 ± 0.229	2.8 ± 0.208	6.37 ± 0.345	3.5 – 4.6 (Wolf <i>et al.</i> , 2014) [12-month time horizon]

Average number of injections delivered to eyes treated for two years after diagnosis, with an experience of therapeutical switch

AMD	Number of intravitreal injections (First drug)	Number of intravitreal injections (Second drug)
AFLIBERCEPT+BEVACIZUMAB	3.66	4.68
RANIBIZUMAB+BEVACIZUMAB	3.66	3.51
BEVACIZUMAB+AFLIBERCEPT	5.87	4.53
BEVACIZUMAB+RANIBIZUMAB	5.39	4.89
BEVACIZUMAB+BROLUCIZUMAB	5.29	3.35
AFLIBERCEPT+RANIBIZUMAB	6.38	4.24
RANIBIZUMAB+AFLIBERCEPT	6.38	5.33
DME	Number of intravitreal injections (First drug)	Number of intravitreal injections (Second drug)
AFLIBERCEPT+BEVACIZUMAB	4.25	3.30
AFLIBERCEPT+DEXAMETHASONE	4.53	2.84
AFLIBERCEPT+RANIBIZUMAB	4.67	3.67
BEVACIZUMAB+AFLIBERCEPT	3.98	4.95
BEVACIZUMAB+DEXAMETHASONE	5.59	1.78
BEVACIZUMAB+RANIBIZUMAB	4.75	4.38
DEXAMETHASONE+AFLIBERCEPT	2.75	4.18
DEXAMETHASONE+BEVACIZUMAB	2.00	6.50
DEXAMETHASONE+FLUOCINOLONE	3.50	1.75
DEXAMETHASONE+RANIBIZUMAB	1.90	4.80
FLUOCINOLONE +RANIBIZUMAB	2.00	2.00
RANIBIZUMAB+AFLIBERCEPT	3.28	3.78
RANIBIZUMAB+BEVACIZUMAB	4.16	3.42
RANIBIZUMAB+DEXAMETHASONE	6.00	1.88
TRIAMCINOLONE+DEXAMETHASONE	1.00	1.50
RVO	Number of intravitreal injections (First drug)	Number of intravitreal injections (Second drug)
AFLIBERCEPT+BEVACIZUMAB	3.00	4.67
AFLIBERCEPT+DEXAMETHASONE	6.54	2.11
AFLIBERCEPT+RANIBIZUMAB	4.00	7.00
DEXAMETHASONE+AFLIBERCEPT	2.54	3.75
RANIBIZUMAB+AFLIBERCEPT	4.58	3.38
RANIBIZUMAB+BEVACIZUMAB	4.25	3.75
RANIBIZUMAB+DEXAMETHASONE	4.00	3.00
CNV	Number of intravitreal injections (First drug)	Number of intravitreal injections (Second drug)
AFLIBERCEPT+RANIBIZUMAB	6.25	5.50
RANIBIZUMAB+AFLIBERCEPT	4.92	4.09

Conclusions

Given the differences between real-life practices and suggested therapeutical schemes, results could support hospitals in the management of maculopathies, revealing the need of optimization strategies (also in preparation to the future introduction of new mechanisms of action and biosimilars of ranibizumab and aflibercept), thus requiring a standardization of the schemes

