Supplementary materials

Effectiveness of Current Treatments for Wet Age-Related Macular Degeneration in Japan: A Systematic Review and Pooled Data Analysis

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Contents

S1 Table. List of 94 articles selected for data extraction

Year	Citation	Number of treatment arms
2008	Iriyama A, Obata R, Inoue Y, Takahashi H, Tamaki Y, Yanagi Y. Effect of posterior juxtascleral triamcinolone acetonide on the efficacy and choriocapillaris hypoperfusion of photodynamic therapy. Graefes Arch *Clin Exp Ophthalmol.* 2008;246:339–344.	2
	Akaza E, Mori R, Yuzawa, M. Long-term results of photodynamic therapy of polypoidal choroidal vasculopathy. *Retina.* 2008;28:717–722.	1
	Kurashige Y, Otani A, Sasahara M, Yodoi Y, Tamura H, Tsujikawa A, et al. Two-year results of photodynamic therapy for polypoidal choroidal vasculopathy. *Am J Ophthalmol.* 2008;146:513–519.	1
	Iwama D, Otani A, Sasahara M, Yodoi Y, Gotoh N, Tamura H, et al. Photodynamic therapy combined with low-dose intravitreal triamcinolone acetonide for age-related macular degeneration refractory to photodynamic therapy alone. *Br J Ophthalmol.* 2008;92:1352–1356.	1
	Dewi NA, Yuzawa M, Tochigi K, Kawamura A, Mori R. Effects of photodynamic therapy on the choriocapillaris and retinal pigment epithelium in the irradiated area. *Jpn J Ophthalmol.* 2008;52:277–281.	3
	Saito M, Iida T, Nagayama D. Photodynamic therapy with verteporfin for age-related macular degeneration or polypoidal choroidal vasculopathy: comparison of the presence of serous retinal pigment epithelial detachment. *Br J Ophthalmol.* 2008;92:1642–1647.	1
	Yamashiro K, Tsujikawa A, Nishida A, Mandai M, Kurimoto Y. Recurrence of polypoidal choroidal vasculopathy after photodynamic therapy. *Jpn J Ophthalmol.* 2008;52:457–462.	1
2009	Mitamura Y, Kubota-Taniai M, Okada K, Kitahashi M, Baba T, Mizunoya S, et al. Comparison of photodynamic therapy to transpupillary thermotherapy for polypoidal choroidal vasculopathy. *Eye (Lond)*. 2009;23:67–72.	1
	Shima C, Gomi F, Sawa M, Sakaguchi H, Tsujikawa M, Tano Y. One-year results of combined photodynamic therapy and intravitreal bevacizumab injection for retinal pigment epithelial detachment secondary to age-related macular degeneration. *Graefes Arch Clin Exp Ophthalmol.* 2009;247:899–906.	1
	Honda S, Imai H, Yamashiro K, Kurimoto Y, Kanamori-Matsui N, Kagotani Y, et al.	2

	Comparative assessment of photodynamic therapy for typical age-related macular degeneration and polypoidal choroidal vasculopathy: a multicenter study in Hyogo prefecture, *Japan. Ophthalmologica*. 2009;223:333–338.	
	Saito K, Yamamoto T, Tsuchiya D, Kawasaki R, Haneda S, Yamashita H. Effect of combined treatment with sub-Tenon injection of triamcinolone acetonide and photodynamic therapy in Japanese patients with age-related macular degeneration. *Jpn J Ophthalmol*. 2009;53:512–518.	4
	Imasawa M, Tsumura T, Sekine A, Kikuchi T, Iijima H. Photodynamic therapy for polypoidal choroidal vasculopathy: baseline perimetric results and visual outcomes. *Jpn J Ophthalmol.* 2009;53:588–592.	1
	Honda S, Kurimoto Y, Kagotani Y, Yamamoto H, Takagi H, Uenishi M. Photodynamic therapy for typical age-related macular degeneration and polypoidal choroidal vasculopathy: a 30-month multicenter study in Hyogo, Japan. *Jpn J Ophthalmol.* 2009;53:593–597.	2
2010	Yamashita A, Shiraga F, Shiragami C, Ono A, Tenkumo K. One-year results of reduced-fluence photodynamic therapy for polypoidal choroidal vasculopathy. *Am J Ophthalmol.* 2010;149:465–471.e1.	1
	Hara R, Kawaji T, Inomata Y, Tahara J, Sagara N, Fukushima M, et al. Photodynamic therapy alone versus combined with intravitreal bevacizumab for neovascular age-related macular degeneration without polypoidal choroidal vasculopathy in Japanese patients. *Graefes Arch Clin Exp Ophthalmol.* 2010;248:931–936.	2
	Sato T, Kishi S, Matsumoto H, Mukai R. Combined photodynamic therapy with verteporfin and intravitreal bevacizumab for polypoidal choroidal vasculopathy. *Am J Ophthalmol.* 2010;149:947–954.e1.	1
	Mori R, Yuzawa M, Lee Z, Haruyama M, Akaza E. Factors influencing visual outcome of polypoidal choroidal vasculopathy one year after photodynamic therapy. *Graefes Arch Clin Exp Ophthalmol.* 2010;248:1233–1239.	1
	Sakurada Y, Kubota T, Imasawa M, Mabuchi F, Tanabe N, Iijima H. Association of LOC387715 A69S genotype with visual prognosis after photodynamic therapy for polypoidal choroidal vasculopathy. *Retina.* 2010;30:1616–1621.	1
2011	Hikichi T, Ohtsuka H, Higuchi M, Matsushita T, Ariga H, Kosaka S, et al. Factors predictive of visual acuity outcomes 1 year after photodynamic therapy in Japanese patients with polypoidal choroidal vasculopathy. *Retina.* 2011;31:857–865.	1

	Akaza E, Yuzawa M, Mori R. Three-year follow-up results of photodynamic therapy for polypoidal choroidal vasculopathy. *Jpn J Ophthalmol.* 2011;55:39–44.	1
	Nakata I, Yamashiro K, Nakanishi H, Tsujikawa A, Otani A, Yoshimura N. VEGF gene polymorphism and response to intravitreal bevacizumab and triple therapy in age-related macular degeneration. *Jpn J Ophthalmol.* 2011;55:435–443.	2
2012	Wakabayashi T, Gomi F, Sawa M, Tsujikawa M, Nishida K. Intravitreal bevacizumab for exudative branching vascular networks in polypoidal choroidal vasculopathy. *Br J Ophthalmol.* 2012;96:394–399.	1
	Tomita K, Tsujikawa A, Yamashiro K, Ooto S, Tamura H, Otani A, et al. Treatment of polypoidal choroidal vasculopathy with photodynamic therapy combined with intravitreal injections of ranibizumab. *Am J Ophthalmol.* 2012;153:68–80.e1.	1
	Nakamura T, Miyakoshi A, Fujita K, Yunoki T, Mitarai K, Yanagisawa S, et al. One-year results of photodynamic therapy combined with intravitreal ranibizumab for exudative age-related macular degeneration. *J Ophthalmol.* 2012;2012:154659.	1
	Nishimura Y, Taguchi M, Nagai T, Fujihara M, Honda S, Uenishi M. Comparison of the effect between pegaptanib and ranibizumab on exudative age-related macular degeneration with small lesion size. *Clin Ophthalmol.* 2012;6:365–368.	2
	Saito M, Iida T, Kano M. Intravitreal ranibizumab for exudative age-related macular degeneration with good baseline visual acuity. *Retina.* 2012;32:1250–1259.	2
	Hikichi T, Higuchi M, Matsushita T, Kosaka S, Matsushita R, Takami K, et al. One-year results of three monthly ranibizumab injections and as-needed reinjections for polypoidal choroidal vasculopathy in Japanese patients. *Am J Ophthalmol.* 2012;154:117–124.e1.	1
	Saito M, Iida T, Kano M. Combined intravitreal ranibizumab and photodynamic therapy for polypoidal choroidal vasculopathy. *Retina.* 2012;32:1272–1279.	1
	Yamazaki T, Koizumi H, Yamagishi T, Kinoshita S. Subfoveal choroidal thickness after ranibizumab therapy for neovascular age-related macular degeneration: 12-month results. *Ophthalmology.* 2012;119:1621–1627.	1
	Nemoto R, Miura M, Iwasaki T, Goto H. Two-year follow-up of ranibizumab combined with photodynamic therapy for polypoidal choroidal vasculopathy. *Clin Ophthalmol.* 2012;6:1633–1638.	1

2013	Yoshida Y, Kohno T, Yamamoto M, Yoneda T, Iwami H, Shiraki K. Two-year results of reduced-fluence photodynamic therapy combined with intravitreal ranibizumab for typical age-related macular degeneration and polypoidal choroidal vasculopathy. *Jpn J Ophthalmol.* 2013;57:283–293.	2
	Hikichi T, Higuchi M, Matsushita T, Kosaka S, Matsushita R, Takami K, et al. Results of 2 years of treatment with as-needed ranibizumab reinjection for polypoidal choroidal vasculopathy. *Br J Ophthalmol*. 2013;97:617–621.	1
	Inoue M, Arakawa A, Yamane S, Kadonosono K. Variable response of vascularized pigment epithelial detachments to ranibizumab based on lesion subtypes, including polypoidal choroidal vasculopathy. *Retina.* 2013;33:990–997.	1
	Saito M, Iida T, Kano M, Itagaki K. Two-year results of combined intravitreal ranibizumab and photodynamic therapy for polypoidal choroidal vasculopathy. *Graefes Arch Clin Exp Ophthalmol*. 2013;251:2099–2110.	2
	Yamamoto A, Okada AA, Sugitani A, Kunita D, Rii T, Yokota R. Two-year outcomes of pro re nata ranibizumab monotherapy for exudative age-related macular degeneration in Japanese patients. *Clin Ophthalmol.* 2013;7:757–763.	2
	Sato T, Kishi S, Matsumoto H, Mukai R. Comparisons of outcomes with different intervals between adjunctive ranibizumab and photodynamic therapy for polypoidal choroidal vasculopathy. *Am J Ophthalmol*. 2013;156:95–105.e1.	2
	Ogino K, Tsujikawa A, Yamashiro K, Ooto S, Oishi A, Nakata I, et al. Intravitreal injection of ranibizumab for recovery of macular function in eyes with subfoveal polypoidal choroidal vasculopathy. Invest *Ophthalmol Vis Sci.* 2013;54:3771–3779.	1
	Saito M, Iida T, Kano M, Itagaki K. Two-year results of intravitreal ranibizumab for polypoidal choroidal vasculopathy with recurrent or residual exudation. *Eye (Lond).* 2013;27:931–939.	1
	Ishibashi T. Maintenance therapy with pegaptanib sodium for neovascular age-related macular degeneration: an exploratory study in Japanese patients (LEVEL-J study). *Jpn J Ophthalmol*. 2013;57:417–423.	1
	Oishi A, Kojima H, Mandai M, Honda S, Matsuoka T, Oh H, et al. Comparison of the effect of ranibizumab and verteporfin for polypoidal choroidal vasculopathy: 12-month LAPTOP study results. *Am J Ophthalmol.* 2013;156:644–651.	2

	Otsuji T, Nagai Y, Sho K, Tsumura A, Koike N, Tsuda M, et al. Initial non-responders to ranibizumab in the treatment of age-related macular degeneration (AMD). *Clin Ophthalmol.* 2013;7:1487–1490.	1
	Sakurada Y, Iijima H. Two-year results of photodynamic therapy with or without intravitreal ranibizumab for polypoidal choroidal vasculopathy. *J Ocul Pharmacol Ther.* 2013;29:832–836.	2
	Inoue M, Arakawa A, Yamane S, Kadonosono K. Long-term outcome of intravitreal ranibizumab treatment, compared with photodynamic therapy, in patients with polypoidal choroidal vasculopathy. *Eye (Lond)*. 2013;27:1013–1020; quiz 1021.	2
2014	Saito M, Iida T, Kano M, Itagaki K. Five-year results of photodynamic therapy with and without supplementary antivascular endothelial growth factor treatment for polypoidal choroidal vasculopathy. *Graefes Arch Clin Exp Ophthalmol.* 2014;252:227–235.	1
	Sakurai M, Baba T, Kitahashi M, Yokouchi H, Kubota-Taniai M, Bikbova G, et al. One-year results of intravitreal ranibizumab combined with reduced-fluence photodynamic therapy for polypoidal choroidal vasculopathy. *Clin Ophthalmol.* 2014;8:235–241.	2
	Yamagishi T, Koizumi H, Yamazaki T, Kinoshita S. Changes in fundus autofluorescence after treatments for polypoidal choroidal vasculopathy. *Br J Ophthalmol.* 2014;98:780–784.	1
	Sawada T, Kakinoki M, Wang X, Kawamura H, Saishin Y, Ohji M. Bimonthly injections of ranibizumab for age-related macular degeneration. *Graefes Arch Clin Exp Ophthalmol.* 2014;252:1545–1551.	1
	Hikichi T, Kitamei H, Shioya S, Higuchi M, Matsushita T, Kosaka S, et al. Relation between changes in foveal choroidal thickness and 1-year results of ranibizumab therapy for polypoidal choroidal vasculopathy. *Br J Ophthalmol.* 2014;98:1201–1204.	1
	Sakai T, Ohkuma Y, Kohno H, Hayashi T, Watanabe A, Tsuneoka H. Three-year visual outcome of photodynamic therapy plus intravitreal bevacizumab with or without subtenon triamcinolone acetonide injections for polypoidal choroidal vasculopathy. *Br J Ophthalmol*. 2014;98:1642–1648.	2
	Inoue M, Arakawa A, Yamane S, Kadonosono K. Intravitreal injection of ranibizumab using a pro re nata regimen for age-related macular degeneration and vision-related quality of life. *Clin Ophthalmol.* 2014;8:1711–1716.	3
	Hata M, Oishi A, Tsujikawa A, Yamashiro K, Miyake M, Ooto S, et al. Efficacy of intravitreal injection of aflibercept in neovascular age-related	2

	macular degeneration with or without choroidal vascular hyperpermeability. *Invest Ophthalmol Vis Sci.* 2014;55:7874–7880.	
2015	Hata M, Tsujikawa A, Miyake M, Yamashiro K, Ooto S, Oishi A, et al. Two-year visual outcome of ranibizumab in typical neovascular age-related macular degeneration and polypoidal choroidal vasculopathy. *Graefes Arch Clin Exp Ophthalmol.* 2015;253:221–227.	2
	Kato A, Yasukawa T, Suga K, Hirano Y, Nozaki M, Yoshida M, et al. Intravitreal ranibizumab for patients with neovascular age-related macular degeneration with good baseline visual acuity. *Ophthalmologica.* 2015;233:27–34.	2
	Hikichi T, Kitamei H, Shioya S. Prognostic factors of 2-year outcomes of ranibizumab therapy for polypoidal choroidal vasculopathy. *Br J Ophthalmol.* 2015;99:817–822.	1
	Oishi A, Tsujikawa A, Yamashiro K, Ooto S, Tamura H, Nakanishi H, et al. One-year result of aflibercept treatment on age-related macular degeneration and predictive factors for visual outcome. *Am J Ophthalmol*. 2015;159:853–860.e1.	1
	Gomi F, Oshima Y, Mori R, Kano M, Saito M, Yamashita A, et al. Initial versus delayed photodynamic therapy in combination with ranibizumab for treatment of polypoidal choroidal vasculopathy: The Fujisan Study. *Retina*. 2015;35:1569–1576.	2
	Yamamoto A, Okada AA, Kano M, Koizumi H, Saito M, Maruko I, et al. One-year results of intravitreal aflibercept for polypoidal choroidal vasculopathy. *Ophthalmology.* 2015;122:1866–1872.	1
	Matsumiya W, Honda S, Otsuka K, Miki A, Nagai T, Imai H, et al. Comparison of the effectiveness and prognostic factors of intravitreal ranibizumab between typical neovascular age-related macular degeneration and polypoidal choroidal vasculopathy over 24 months of follow-up. *Ophthalmologica.* 2015;234:33–39.	2
2016	Kuroda Y, Yamashiro K, Tsujikawa A, Ooto S, Tamura H, Oishi A, et al. Retinal pigment epithelial atrophy in neovascular age-related macular degeneration after ranibizumab treatment. *Am J Ophthalmol*. 2016;161:94–103.e1.	2
	Koizumi H, Kano M, Yamamoto A, Saito M, Maruko I, Sekiryu T, et al. Subfoveal choroidal thickness during aflibercept therapy for neovascular age-related macular degeneration: twelve-month results. *Ophthalmology*. 2016;123:617–624.	2
	Inoue M, Yamane S, Taoka R, Arakawa A, Kadonosono K. Aflibercept for polypoidal choroidal vasculopathy: as needed versus fixed interval dosing. *Retina.* 2016;36:1527–1534.	2

	Suzuki M, Nagai N, Shinoda H, Uchida A, Kurihara T, Tomita Y, et al. Distinct responsiveness to intravitreal ranibizumab therapy in polypoidal choroidal vasculopathy with single or multiple polyps. *Am J Ophthalmol*. 2016;166:52–59.	2
	Kikushima W, Sakurada Y, Sugiyama A, Tanabe N, Kume A, Iijima H. Factors predictive of visual outcome 1 year after intravitreal aflibercept injection for typical neovascular age-related macular degeneration. *J Ocul Pharmacol Ther*. 2016;32:376–382.	2
	Sakai T, Okano K, Kohno H, Tsuneoka H. Three-year visual outcomes of intravitreal ranibizumab with or without photodynamic therapy for polypoidal choroidal vasculopathy. *Acta Ophthalmol.* 2016;94:e765–e771.	2
	Inoue M, Yamane S, Sato S, Sakamaki K, Arakawa A, Kadonosono K. Comparison of time to retreatment and visual function between ranibizumab and aflibercept in age-related macular degeneration. *Am J Ophthalmol.* 2016;169:95–103.	2
2017	Kikushima W, Sakurada Y, Sugiyama A, Tanabe N, Kume A, Iijima H. Comparison of initial treatment between 3-monthly intravitreal aflibercept monotherapy and combined photodynamic therapy with single intravitreal aflibercept for polypoidal choroidal vasculopathy. *Graefes Arch Clin Exp Ophthalmol.* 2017;255:311–316.	2
	Saito M, Kano M, Itagaki K, Sekiryu T. Efficacy of intravitreal aflibercept in Japanese patients with exudative age-related macular degeneration. *Jpn J Ophthalmol*. 2017;61:74–783.	2
	Kikushima W, Sakurada Y, Sugiyama A, Tanabe N, Yoneyama S, Iijima H. Retreatment of polypoidal choroidal vasculopathy after photodynamic therapy combined with intravitreal ranibizumab. *Jpn J Ophthalmol.* 2017;61:61–66.	1
	Matsumiya W, Honda S, Otsuka K, Miki A, Nagai T, Imai H, et al. One-year outcome of combination therapy with intravitreal aflibercept and verteporfin photodynamic therapy for polypoidal choroidal vasculopathy. *Graefes Arch Clin Exp Ophthalmol.* 2017;255:541–548.	1
	Ohnaka M, Nagai Y, Sho K, Miki K, Kimura M, Chihara T, et al. A modified treat-and-extend regimen of aflibercept for treatment-naive patients with neovascular age-related macular degeneration. *Graefes Arch Clin Exp Ophthalmol.* 2017;255:657–664.	2
	Hosokawa M, Morizane Y, Hirano M, Kimura S, Kumase F, Shiode Y, et al. One-year outcomes of a treat-and-extend regimen of intravitreal aflibercept for polypoidal choroidal vasculopathy. *Jpn J Ophthalmol*. 2017;61:150–158.	1

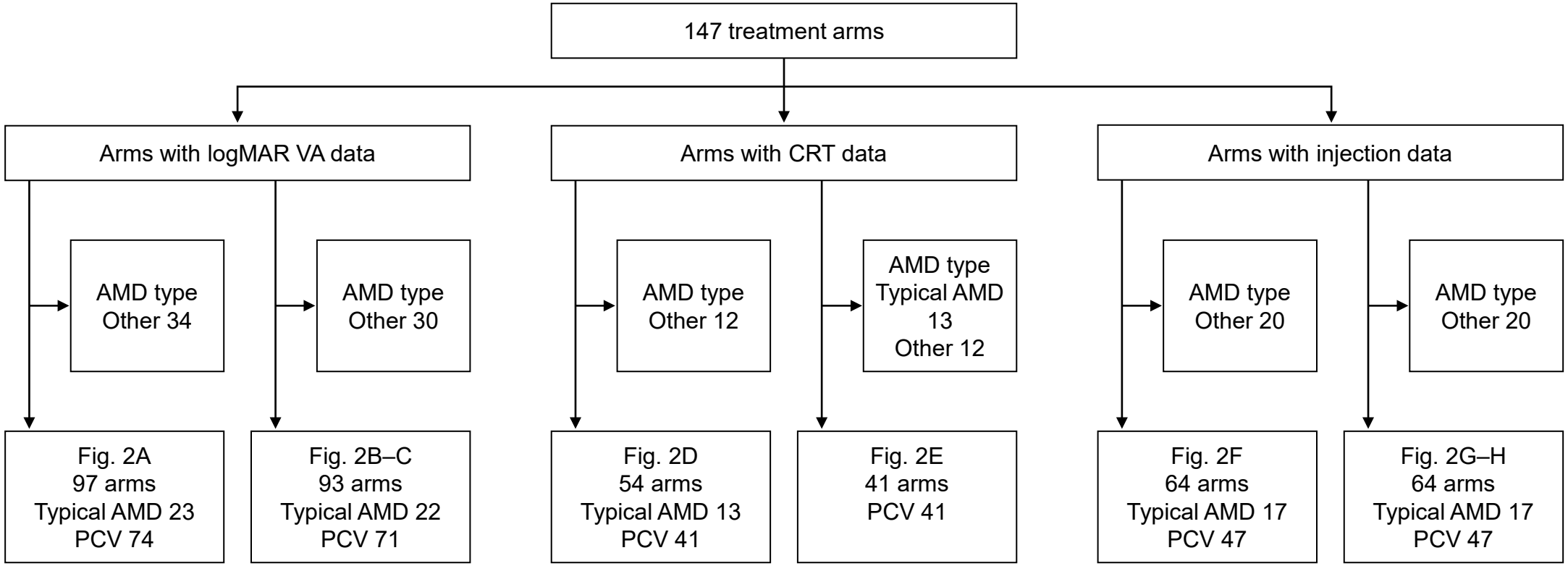
	Takayama K, Kaneko H, Sugita T, Maruko R, Hattori K, Ra E, et al. One-year outcomes of 1 + pro re nata versus 3 + pro re nata intravitreal aflibercept injection for neovascular age-related macular degeneration. *Ophthalmologica*. 2017;237:105–110.	2
	Yamamoto A, Okada AA, Nakayama M, Yoshida Y, Kobayashi H. One-year outcomes of a treat-and-extend regimen of aflibercept for exudative age-related macular degeneration. *Ophthalmologica*. 2017;237:139–144.	1
	Kikushima W, Sakurada Y, Yoneyama S, Sugiyama A, Tanabe N, Kume A, et al. Incidence and risk factors of retreatment after three-monthly aflibercept therapy for exudative age-related macular degeneration. *Sci Rep.* 2017;7:44020.	2
	Nakai S, Honda S, Miki A, Matsumiya W, Nakamura M. Comparison of the 12-month outcomes of intravitreal ranibizumab between two angiographic subtypes of polypoidal choroidal vasculopathy. *Ophthalmologica.* 2017;237:123–127.	2
	Mori R, Tanaka K, Haruyama M, Kawamura A, Furuya K, Yuzawa M. Comparison of pro re nata versus bimonthly injection of intravitreal aflibercept for typical neovascular age-related macular degeneration. *Ophthalmologica*. 2017;238:17–22.	2
	Takayama K, Kaneko H, Kataoka K, Hattori K, Ra E, Tsunekawa T, et al. Comparison between 1-year outcomes of aflibercept with and without photodynamic therapy for polypoidal choroidal vasculopathy: retrospective observation study. *PLoS One.* 2017;12:e0176100.	2
	Arakawa A, Inoue M, Sato S, Yamane S, Kadonosono K. Efficacy of intravitreal aflibercept injections for Japanese patients with polypoidal choroidal vasculopathy. *Clin Ophthalmol.* 2017;11:797–802.	1
	Oshima Y, Kimoto K, Yoshida N, Fujisawa K, Sonoda S, Kubota T, et al. One-year outcomes following intravitreal aflibercept for polypoidal choroidal vasculopathy in Japanese patients: the APOLLO study. *Ophthalmologica.* 2017;238:163–171.	1
	Ito A, Matsumoto H, Morimoto M, Mimura K, Akiyama H. Two-year outcomes of a treat-and-extend regimen using intravitreal aflibercept injections for typical age-related macular degeneration. *Ophthalmologica.* 2017;238:236–242.	1
	Kikushima W, Sakurada Y, Sugiyama A, Yoneyama S, Tanabe N, Matsubara M, et al. Comparison of two-year outcomes after photodynamic therapy with ranibizumab or aflibercept for polypoidal choroidal vasculopathy. *Sci Rep.* 2017;7:16461.	2

2018	Hikichi T. Six-year outcomes of antivascular endothelial growth factor monotherapy for polypoidal choroidal vasculopathy. *Br J Ophthalmol*. 2018;102:97–101.	1
	Kuroda Y, Yamashiro K, Ooto S, Tamura H, Oishi A, Nakanishi H, et al. Macular atrophy and macular morphology in aflibercept-treated neovascular age-related macular degeneration. *Retina.* 2018;38:1743–1750.	1
	Maruyama-Inoue M, Sato S, Yamane S, Kadonosono K. Intravitreal injection of aflibercept in patients with polypoidal choroidal vasculopathy: a 3-year follow-up. *Retina.* 2018;38:2001–2009.	2
	Sugiyama A, Sakurada Y, Honda S, Miki A, Matsumiya W, Yoneyama S, et al. Retreatment of exudative age-related macular degeneration after loading 3-monthly intravitreal ranibizumab. *Ophthalmologica.* 2018;239:52–59.	2
	Sakurada Y, Kikushima W, Sugiyama A, Yoneyama S, Tanabe N, Matsubara M, et al. AREDS simplified severity scale as a predictive factor for response to aflibercept therapy for typical neovascular age-related macular degeneration. *Graefes Arch Clin Exp Ophthalmol*. 2018;256:99–104.	3
	Haga A, Kawaji T, Ideta R, Inomata Y, Tanihara H. Treat-and-extend versus every-other-month regimens with aflibercept in age-related macular degeneration. *Acta Ophthalmol.* 2018;96:e393–e398.	2
	Sakai T, Okude S, Tsuneoka H. Foveal threshold and photoreceptor integrity for prediction of visual acuity after intravitreal aflibercept on age-related macular degeneration. *Clin Ophthalmol.* 2018;12:719–725.	1
	Miyata M, Ooto S, Yamashiro K, Tamura H, Hata M, Ueda-Arakawa N, et al. Five-year visual outcomes after anti-VEGF therapy with or without photodynamic therapy for polypoidal choroidal vasculopathy. *Br J Ophthalmol*. 2019;103:617–622.[a]	2
	Hara C, Wakabayashi T, Toyama H, Fukushima Y, Sayanagi K, Sato S, et al. Characteristics of patients with neovascular age-related macular degeneration who are non-responders to intravitreal aflibercept. *Br J Ophthalmol*. 2019;103:627–629.[a]	1
	Sakamoto S, Takahashi H, Inoue Y, Arai Y, Inoda S, Kakinuma N, et al. Intravitreal aflibercept for exudative age-related macular degeneration with good visual acuity: 2-year results of a prospective study. *Clin Ophthalmol*. 2018;12:1137–1147.	2
	Ogasawara M, Koizumi H, Yamamoto A, Itagaki K, Saito M, Maruko I, et al. Prognostic factors after aflibercept therapy for typical age-related	2

	macular degeneration and polypoidal choroidal vasculopathy. *Jpn J Ophthalmol*. 2018;62:584–591.	
	Ono A, Shiragami C, Manabe S, Takasago Y, Osaka R, Kobayashi M, et al. One-year outcomes of fixed treatment of intravitreal aflibercept for exudative age-related macular degeneration and the factor of visual prognosis. *Medicine (Baltimore)*. 2018;97:e11737.	2
	Morizane-Hosokawa M, Morizane Y, Kimura S, Shiode Y, Hirano M, Doi S, et al. Impact of polyp regression on 2-year outcomes of intravitreal aflibercept injections: a treat-and-extend regimen for polypoidal choroidal vasculopathy. *Acta Med Okayama*. 2018;72:379–385.	1

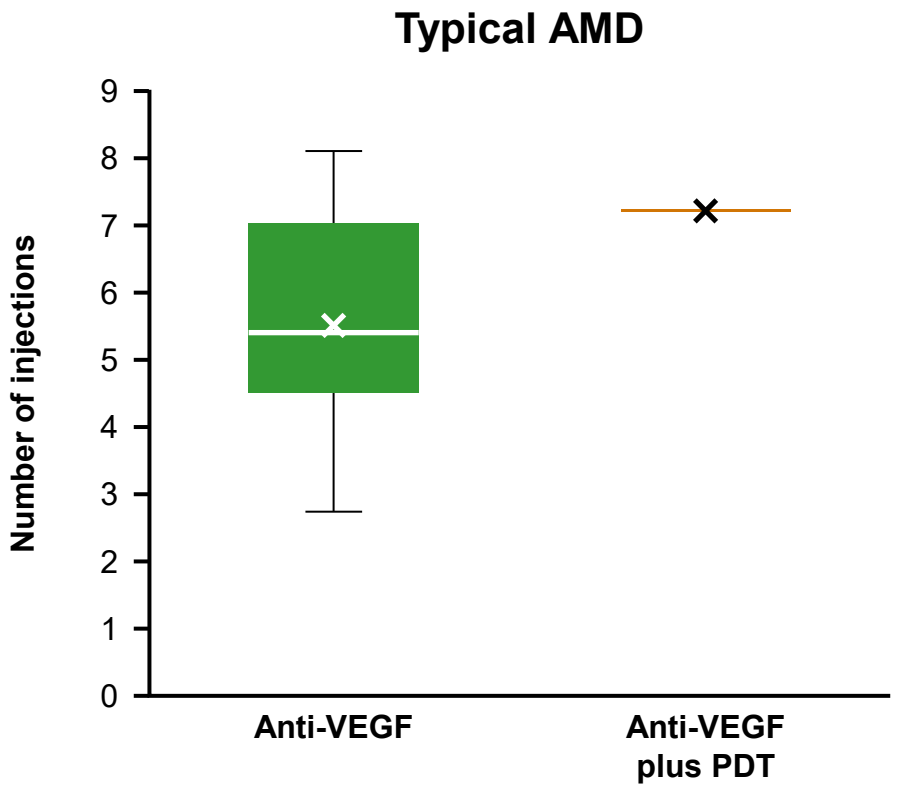
[a]Available as an epublication in 2018 and thus eligible for inclusion in the analysis, although the formal print publication date was 2019.

S1 Fig. Treatment arms included in outcome calculations.



AMD: age-related macular degeneration; CRT: central retinal thickness; logMAR: logarithm of the minimum angle of resolution; PCV: polypoidal choroidal vasculopathy; VA: visual acuity.

S2 Fig. Number of anti-VEGF injections stratified by disease type (typical AMD) and treatment modality.



Mean (median) number of injections	Anti-VEGF	Anti-VEGF plus PDT
During the first 12 months of treatment	5.5 (5.4)	7.2 (7.2)
Treatment groups (n)	16	1

AMD: age-related macular degeneration; PDT: photodynamic therapy; VEGF: vascular endothelial growth factor

S1 Text. PRISMA checklist

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	p1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	p3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	P4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	P5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	P6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	P5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	P5 and S1 Text
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	P6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	P6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	P6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	P6-7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	P6-7

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	P7 and Fig 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	P7 and Table S1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	P8-9, Figs 2A-G, and S2 Fig
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	P9-10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	p10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	p11
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	p13

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097 For more information, visit: **www.prisma-statement.org**.

S2 Text. Search strings

Search string 1: “Wet Age-Related Macular Degeneration”[MeSH] OR “Neovascular Age-Related Macular Degeneration”[MeSH] OR “Exudative Age-Related Macular Degeneration”[MeSH] OR “Wet Age-Related Macular Degeneration”[TIAB] OR “Neovascular Age-Related Macular Degeneration”[TIAB] OR “Exudative Age-Related Macular Degeneration”[TIAB] OR “typical age related macular degeneration”[TIAB] OR “polypoidal choroidal vasculopathy”[TIAB] OR “retinal angiomatous proliferation”[TIAB] OR “classic choroidal neovascularization”[TIAB] OR “occult choroidal neovascularization”[TIAB] OR “pachychoroid neovascularization”[TIAB] OR “type1 choroidal neovascularization”[TIAB] OR “type2 choroidal neovascularization”[TIAB].

Search string 2: epidemi*[TIAB] OR “analyses, demographic”[MeSH] OR demographic*[TIAB] OR inciden*[TIAB] OR prevalen*[TIAB] OR strain*[TIAB] OR burden[TIAB] OR severity[TIAB] OR cost-effectiveness[TIAB] OR cost[TIAB] OR “cost, treatment”[MeSH] “health care resource”[TIAB] OR “burden of illness”[MeSH] OR “burden of illness”[TIAB] OR “analyses, cost”[MeSH] OR DALY[TIAB] OR QALY[TIAB] OR utility[TIAB] OR cost-utility[TIAB] OR effectiveness[TIAB] OR “Quality of life”[TIAB] OR QoL[TIAB] OR PRO[TIAB] OR treatment[TIAB] OR "clinical effectiveness"[TIAB] OR “disease management”[TIAB] OR guideline[TIAB] OR therapy[TIAB] OR “clinical study”[TIAB] OR “clinical trial”[TIAB] OR ranibizumab[TIAB] OR pegaptanib[TIAB] OR aflibercept[TIAB] OR bevacizumab[TIAB] OR “photodynamic therapy”[TIAB].

Search string 3: Japan*.

The three strings were combined with the language and date limitations to produce the first group of articles for evaluation. Reviews were scanned for details of additional relevant studies. The gray literature was also evaluated, including some Japanese language publications, by searching treatment guidelines and papers published by major government webpages and academic

associations, including the Japanese Ophthalmological Society; Japan Ophthalmologists Association; Ministry of Health, Labour and Welfare; Japan Society for Laser Surgery and Medicine; and Japan Intractable Diseases Information Center.