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Cumulative Experience of Extended Wear Clinical Trials of a Silicone Hydrogel Contact Lens

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Introduction

The landmark CLI study of 1989 identified the occurrence of microbial keratitis (MK) as 4 in 10,000 for DW and 21 in 10,000 for EW [1]. This translates into incidence rates of 0.04% and 0.21%, respectively. These figures are the most referenced values cited in the professional literature today. The incidence of MK in EW is perceived by some to represent an unacceptably high risk of serious, sight-threatening adverse events, and as such, have served to curtail the active fitting of extended wear by many practitioners.

The launch of silicone hydrogel contact lenses, however, has ushered in a new era of continuous wear. Eye care practitioners, as well as potential wearers, have approached this previously popular modality with caution based on the historical record and negative perceptions of extended wear with conventional hydrogel lenses. The key concern of the profession regarding this modality is incidence of microbial keratitis (MK).

Previous reports provide evidence of the clinical benefits derived from the improved oxygen performance of silicone-hydrogel lenses (PureVision). Relative to a conventional hydrogel extended wear control lens, physiological correlates of hypoxia; microcysts, striae, ocular redness, neovascularization and epithelial edema, were reduced and/or eliminated. Non-infectious inflammatory events, in the form of tarsal conjunctival changes and corneal infiltrates occurred at similar rates and do not appear to be related to hypoxia.[2]

The purpose of this poster is to report the cumulative experience of controlled extended wear clinical trials for PureVision (balafilcon A) contact lenses with regard to patient-years and incidence of microbial keratitis.

Methods

Bausch & Lomb Clinical Research conducted 27 controlled extended wear clinical trials under GCP guidelines. All patients were fitted with PureVision lenses manufactured from a highly oxygen permeable, low water content (36%), surface treated silicone hydrogel material, balafilcon A. At the conclusion of the studies, the results were analyzed for the presence of serious adverse events including MK. Microbial keratitis was defined as presenting with the following:

- large central corneal infiltrate with overlaying epithelial defect
- associated symptoms (e.g. pain, redness)
- may or may not culture positive
- anterior chamber reaction
- vision loss due to corneal scarring.

	Material	Power	BC/Dia Dk/t*
PureVision lenses:	balafilcon A	+4.00 to -9.00	8.6/14.0 112

Results

Nearly 4,800 patients completed 27 extended wear studies. These studies ranged in length from 2 weeks to 12 months, for a cumulative duration of 138 months (11.5 years), and provide over 2,200 patient-years of data and experience. Seven studies, including more than 2,100 patients, were 12 months in duration.

There were no reports of MK or other serious sight-threatening adverse events. Other clinical signs were within expected norms.

# of EW studies	Study duration	Patients enrolled	Patients completed	Patient-years
7	12 month	2145	1546	1546
4	6 month	829	706	353
5	3 month	518	427	108
11	< 3 month	2281	2119	203
27	-	**5773**	**4798**	**2210**

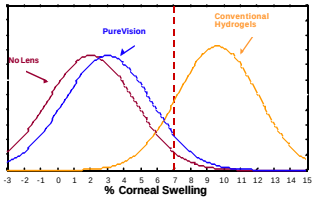
Discussion

Improving the safety profile of an extended wear contact lens, may be defined by the significant reduction, or elimination of the incidence of serious sight threatening adverse events (e.g. MK). It is widely recognized that improving the oxygen performance of soft lenses will not, by itself, eradicate MK. Hypoxia is, however, considered to be a significant factor contributing to the appropriate conditions for infectious keratitis. Minimizing hypoxia, therefore, should reduce the potential for MK.

Overnight corneal swelling:

Previous reports have shown that, relative to conventional hydrogel EW materials, lenses manufactured from balafilcon A cause less corneal swelling (see Figure 1). Indeed, levels of overnight corneal swelling with PureVision lenses is equivalent to wearing no lenses.[3]

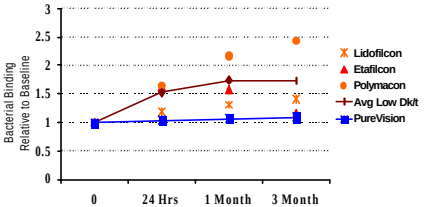
Figure 1 - Overnight Corneal Swelling



Bacterial binding:

Another important finding is that continuous wear of ultra-high Dk/t silicone hydrogel lenses has demonstrated reduced bacterial binding to epithelial cells compared to conventional hydrogel extended wear lenses (see Figure 2).[4]

Figure 2† - Epithelial Cell Bacterial Binding



[† Adapted with permission of the authors.]

Both of these factors, hypoxia and bacterial binding, typically considered risk factors to developing a serious sight-threatening adverse event such as MK, have been eliminated, or significantly reduced with PureVision lenses.

Cumulative clinical experience:

The results of this analysis yielded no reported cases of microbial keratitis in 2,210 patient-years of experience. This suggests that the incidence of MK in overnight wear of PureVision lenses may be significantly less than that reported in the landmark Contact Lens Institute (CLI) study. While an accurate figure of MK incidence will not be established until such time there is extensive data from both clinical trials and market experience, based on the conclusion of the CLI study, and on the number of patient-years (>2,200) accumulated in our extended wear clinical trials, one would have expected to observe up to five events of MK.

This reduced rate in controlled clinical trials appears to reflect market experience. Post-market surveillance reported by Bausch & Lomb medical vigilance, was audited to identify likely cases of microbial keratitis. Beginning in 1999 through November 2001, Bausch & Lomb's global medical surveillance group has registered only four cases that meet the criteria of microbial keratitis.

With more than 200,000 PureVision wearers worldwide, if all events occurred in the same year, the incident rate would be 0.0015%. To gain a conservative estimate of incident rate, assuming a number of events go unreported, the above rate, if multiplied by a factor of 10, only equals 0.015%. In comparison to the rates calculated from the results of the CLI study (0.21% for extended wear and 0.04% for daily wear), it appears that the incident rate of MK for PureVision lenses, utilized in all modalities, is tracking dramatically lower.

Conclusion

Silicone hydrogel technology is a significant step forward for the soft contact lens industry. The cumulative experience of Bausch & Lomb's Clinical Research suggests that the incidence of microbial keratitis will be less than that reported in the landmark CLI study of conventional hydrogel lenses. As such, practitioners may be confident with respect to the safety of this new generation of soft contact lenses for continuous wear.

References

- Schein, OD, et al: The relative risk of ulcerative keratitis among users of daily-wear and extended-wear soft contact lenses. A case-control study. *N Engl J Med* 1989;321:773-778.
- Comstock, TL, Crescuillo, TA, Dey, D, Scheurich, L: One-year prospective clinical trial of balafilcon A (PureVision) soft contact lenses when used on a 30-day continuous wear schedule. *AAO International Meeting Poster, 2000.*

3. Comstock, TL, Robboy, MW, Cox, IG, Brennan, NA: Overnight Clinical Performance of a High Dk Silicone Hydrogel Soft Contact Lens (balafilcon A) compared to a conventional extended wear lens (etafilcon A). *BCLA Poster, 1999.*
4. Ren DH, Petroll WM, Jester JV, Ho-Fan J, Cavanagh HD. The relationship between contact lens oxygen permeability and binding of *Pseudomonas aeruginosa* to human corneal epithelial cells after overnight and extended wear. *CLAO* 1999;25(2);80-100.

* Dk/t for –3.00D lens based on polarographic method: non-edge corrected