**Appendix 1: PICO Search Strategy**

Q1) Are SED more effective at treating patients with ocular surface disease, than conventional treatment?

|  |  |  |  |
| --- | --- | --- | --- |
| Population | Intervention | Comparison  | Outcome |
| Patients with Oculare Surface Disease | Serum Eye Drops | Conventional treatment |  |
| Sjögren's Syndrome related dry eye, Mucous Membrane Pemphigoid, Stevens‐Johnson‐Syndrome, Graft Versus Host Disease, Ulcerative keratitis, neurotrophic cornea, diabetic cornea, persistent epithelial defects, ocular surface reconstruction surgery, supportive therapy | * Serum or Cord Blood or Plasma or Blood Products

AND* Autologous or allogeneic

ANDeyedrops | Artificial TearsOcular LubricantsCarmelloseHyaluronates | Clinical:* Ocular Surface Disease index, tear film break-up time, Schirmer's Test, Osmolarity, Oxford staining Score, Ocular Surface Staining Score, Visual acuity, Near Vison, Radner Read Speed

Laboratory:HLA DR2, impression cytology, cytokines, goblet cells, mucin, gene expression, proteonomics, metabolomics |

Q2) Is there evidence of superiority in the cost and clinical effectiveness of autologous serum eye drops (Auto-SED) versus allogeneic serum eye drops (Allo-SED) at treating patients with ocular surface disease?

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| --- | --- | --- | --- |
| Population | Intervention | Comparison  | Outcome |
| Patients with Ocular Surface Disease | Serum Eye Drops | Serum Eye Drops |  |
| Sjögren's Syndrome related dry eye, Mucous Membrane Pemphigoid, Stevens‐Johnson‐Syndrome, Graft Versus Host Disease, Ulcerative keratitis, neurotrophic cornea, diabetic cornea, persistent epithelial defects, ocular surface reconstruction surgery, supportive therapy | Autologous Serum Eye Drops | Allogeneic Serum Eye DropsClinical Trial | Clinical:* Ocular Surface Disease index, tear film break-up time, Schirmer's Test, Osmolarity, Oxford staining Score, Ocular Surface Staining Score, Visual acuity, Near Vison, Radner Read Speed

Laboratory:- HLA DR2, impression cytology, cytokines, goblet cells, mucin, gene expression, proteonomics, metabolomicsDirect CostIndirect CostEQ5D |

Q3) What effect does dose size have on the effect of treatment with SED for patients with ocular surface disease?

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| --- | --- | --- | --- |
| Population | Intervention | Comparison  | Outcome |
| Patients with Ocular Surface Disease | Serum Eye Drops |  |  |
| Sjögren's Syndrome related dry eye, Mucous Membrane Pemphigoid, Stevens‐Johnson‐Syndrome, Graft Versus Host Disease, Ulcerative keratitis, neurotrophic cornea, diabetic cornea, persistent epithelial defects, ocular surface reconstruction surgery, supportive therapy | Autologous allogeneicSerum Eye DropsDose | Clinical Trial, Case series, case reports | Clinical:* Ocular Surface Disease index, tear film break-up time, Schirmer's Test, Osmolarity, Oxford staining Score, Ocular Surface Staining Score, Visual acuity, Near Vison, Radner Read Speed

Laboratory:HLA DR2, impression cytology, cytokines, goblet cells, mucin, gene expression, proteonomics, metabolomics |

Q4) What effect does concentration of formulation have on the effect of treatment with SED for patients with ocular surface disease?

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| --- | --- | --- | --- |
| Population | Intervention | Comparison  | Outcome |
| Patients with Ocular Surface Disease | Serum Eye Drops |  |  |
| Sjögren's Syndrome related dry eye, Mucous Membrane Pemphigoid, Stevens‐Johnson‐Syndrome, Graft Versus Host Disease, Ulcerative keratitis, neurotrophic cornea, diabetic cornea, persistent epithelial defects, ocular surface reconstruction surgery, supportive therapy | Autologous allogeneicSerum Eye DropsFormulation ConcentrationDilutionPreparation | Clinical Trial, case reports, series | Clinical:* Ocular Surface Disease index, tear film break-up time, Schirmer's Test, Osmolarity, Oxford staining Score, Ocular Surface Staining Score, Visual acuity, Near Vison, Radner Read Speed

Laboratory:HLA DR2, impression cytology, cytokines, goblet cells, mucin, gene expression, proteonomics, metabolomics |

Q5) What effect does duration of treatment have on the effect of treatment with SED for patients with ocular surface disease?

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| --- | --- | --- | --- |
| Population | Intervention | Comparison  | Outcome |
| Patients with Ocular Surface Disease | Serum Eye Drops |  |  |
| Sjögren's Syndrome related dry eye, Mucous Membrane Pemphigoid, Stevens‐Johnson‐Syndrome, Graft Versus Host Disease, Ulcerative keratitis, neurotrophic cornea, diabetic cornea, persistent epithelial defects, ocular surface reconstruction surgery, supportive therapy | Autologous allogeneicSerum Eye DropsDurationTreatment | Clinical Trial, case reports, series | Clinical:* Ocular Surface Disease index, tear film break-up time, Schirmer's Test, Osmolarity, Oxford staining Score, Ocular Surface Staining Score

Laboratory:HLA DR2, impression cytology, cytokines, goblet cells, mucin, gene expression, proteonomics, metabolomics |

Q6) What effect does frequency of treatment have on the effect of treatment with SED for patients with ocular surface disease?

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| --- | --- | --- | --- |
| Population | Intervention | Comparison  | Outcome |
| Patients with Ocular Surface Disease | Serum Eye Drops |  |  |
| Sjögren's Syndrome related dry eye, Mucous Membrane Pemphigoid, Stevens‐Johnson‐Syndrome, Graft Versus Host Disease, Ulcerative keratitis, neurotrophic cornea,diabetic cornea, persistent epithelial defects, ocular surface reconstruction surgery, supportive therapy | Autologous allogeneicSerum Eye DropsDurationTreatmentNumber of drops | Clinical Trial, case reports, series | Clinical:* Ocular Surface Disease index, tear film break-up time, Schirmer's Test, Osmolarity, Oxford staining Score, Ocular Surface Staining Score, Visual acuity, Near Vison, Radner Read Speed

Laboratory:HLA DR2, impression cytology, cytokines, goblet cells, mucin, gene expression, proteonomics, metabolomics |

Q7) Which clinical outcome measures best record the treatment effect for monitoring ocular surface disease?

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| --- | --- | --- | --- |
| Population | Intervention | Comparison  | Outcome |
| Patients with Ocular Surface Disease | Serum Eye Drops |  |  |
| Sjögren's Syndrome related dry eye, Mucous Membrane Pemphigoid, Stevens‐Johnson‐Syndrome, Graft Versus Host Disease, Ulcerative keratitis, neurotrophic cornea, diabetic cornea, persistent epithelial defects, ocular surface reconstruction surgery, supportive therapy | Autologous allogeneicSerum Eye Drops | Clinical trials, case reports, series | Clinical:* Ocular Surface Disease index, tear film break-up time, Schirmer's Test, Osmolarity
* Anxiety, Depression, Quality of Life
* Laboratory:

HLA DR2, impression cytology, cytokines, goblet cells, mucin  |

Q8) Which patient reported outcome measures best record the treatment effect for monitoring impact on patient debility?

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| --- | --- | --- | --- |
| Population | Intervention | Comparison  | Outcome |
| Patients with Ocular Surface Disease | Serum Eye Drops |  |  |
| Sjögren's Syndrome related dry eye, Mucous Membrane Pemphigoid, Stevens‐Johnson‐Syndrome, Graft Versus Host Disease, Ulcerative keratitis, neurotrophic cornea, diabetic cornea, persistent epithelial defects, ocular surface reconstruction surgery, supportive therapy |  | Epidemiiological studies, metanalysis, case reports, series | Ocular Surface Disease index (OSDI,NEI VFQ, Dry Eye Question (DEQ), impact of dry eye on everyday life (IDEEL) questionnaire, International Sjogren’s classification, Hospital Anxiety and Depression Score |