Supplementary Information: Comprehensive characterization of central BCL-2 family members in aberrant eosinophils and their impact on therapeutic strategies

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Supplementary Information: Figures

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Supplementary Figure 1:
Interleukin-5 (IL-5) blood plasma levels at baseline did not influence the response to BH3-mimetic treatment in 72h viability assays. Viability data from aberrant eosinophils (see Figure 3) were correlated by Pearson correlation with IL-5 in blood plasma levels at the timepoint of sampling. The functional relation was described with linear regression. (A-D) show the relation between IL-5 absorbance levels and viability after 72h treatment with ABT-199, ABT-737, S63845, WEHI-539, each at 1µM. Pearson r, p-values and linear regression terms are indicated.
Supplementary Figure 2:
IL-5 blood plasma levels at baseline do not correlate with the expression level of BIM or Morbid. (A, B) Gene expression data from aberrant and healthy eosinophils (see Figure 1) were correlated by Pearson correlation with IL-5 in blood plasma levels at the timepoint of sampling. The functional relation was described with linear regression. Pearson r, p-values and linear regression terms are indicated.
Supplementary Figure 3:
Supplement of Figure 3 (main text): Aberrant eosinophilic granulocytes from patients with hypereosinophilic disorders are more resistant to apoptosis induction with BH₃-mimetics than healthy eosinophils. (A) Viable granulocytes of 13 healthy, age-matched controls and of 38 patients (HE; reactive eosinophilia n=1, L-HES n=2, MLN-Eo n=1, CEL-NOS n=8, EGPAⁿca⁻ n=9) were treated for 72h with ABT-737 1µM and DMSO soluble control and gated on Siglec8+ granulocytes. Cell viability was measured by flow cytometry using Annexin V and 7AAD staining, a ratio of inhibitory treatment to DMSO soluble control is shown with mean ± standard deviation (SD). Data were especially tested for differences between the healthy and the EGPAⁿca⁻ patient group. Kruskal-Wallis test and post-hoc pairwise comparison was applied, the p-values are indicated. (B) Viable granulocytes of 13 healthy, age-matched controls and of 35 patients (HE; reactive eosinophilia n=1, HES n=15, L-HES n=2, MLN-Eo n=1, CEL-NOS n=7, EGPAⁿca⁻ n=9) were treated for 72h with S63845 1µM and DMSO soluble control and gated on Siglec8+ granulocytes. Cell viability was measured by flow cytometry using Annexin V and 7AAD staining, a ratio of inhibitory treatment to DMSO soluble control is shown with mean ± standard deviation (SD). The analysed cohort was subdivided according to the result of the 72h viability assay. Good responders were classified when viability was < 60%, bad responders when viability was >60%. Kruskal-Wallis test and post-hoc pairwise comparison was used, p-values are indicated.
Supplementary Figure 4:
Shown is an example of the FACS analysis gating strategy for viability analysis. After excluding cell debris (1 and 2), Siglec-8+ eosinophils (3) are gated. Cell death was measured by flow cytometry of Annexin V (FITC) and 7-aminoactinomycin D (7AAD; PerCP). Viable cells were negative for both Annexin and 7AAD (4, sector Q4).
Supplementary Information: Tables

Comprehensive characterization of central BCL-2 family members in aberrant eosinophils and their impact on therapeutic strategies
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Supplementary Table 1:
Clinical and molecular characteristics of hypereosinophilic patients contributing samples. Age, sex, WHO category, maximal eosinophil count (in % of the total leucocyte count and absolute eosinophil count ), location of clinical manifestation and additional information were documented for each patient sample. Criteria for hypereosinophilia and hypereosinophilic syndromes were applied as defined in the WHO Update 2019. m = male, f = female, HES = hypereosinophilic syndrome, L-HES = lymphocyte variant hypereosinophilic syndrome, MLN-Eo = eosinophilia-associated myeloproliferative neoplasia, CEL-NOS = chronic eosinophilic leukemia not otherwise specified, EGPA = eosinophilic granulomatosis with polyangiitis, Eos = Eosinophil granulocytes, BMMCs = Bone marrow mononuclear cells, R-CHOP = rituximab/cyclophosphamide/hydroxydaunorubicin/ vincristine/prednisone, NA= not available, GI = gastrointestinal tract, PNS = peripheral nervous system, ENT = ear, nose, throat, BM = bone marrow, AKI = acute kidney injury, DLBCL = diffuse large B-cell lymphoma, ANCA = anti-neutrophil cytoplasmatic antibody.
| ID | Age | Sex | Type of Hypersensitivity | Max. (%) Eosinophils in Blood | Max. Eosinophils (G/L) | IL-5 level (absorbance) | Viability Eos (NDMOSO) after 72h ABT-199 | Viability Eos (NDMOSO) after 72h ABT-737 | Viability Eos (NDMOSO) after 72h VN5-339 | Viability Eos (NDMOSO) after 72h ANT1-399 | Viability BMCCs (NDMOSO) after 72h ABT-199 | Viability BMCCs (NDMOSO) after 72h ABT-737 | Viability BMCCs (NDMOSO) after 72h VN5-339 | Viability BMCCs (NDMOSO) after 72h ANT1-399 | Viability BMCCs (NDMOSO) after 72h VEN1-42 | (Pre-)Treatment | Location of Main Lymphoma / Eosinophil Infiltration | Comment |
|----|-----|-----|--------------------------|-----------------------------|------------------------|------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| 1  | 66  | m   | reactive                | 72                           | 3.9                    | NA                     | 70.59                          | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | corticosteroids                | Gl                              | Primary sclerosing cholangitis  |
| 2  | 60  | f   | reactive                | 25                           | 2.5                    | NA                     | 91.81                          | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | corticosteroids                | Gl                              | skin                            |
| 3  | 27  | f   | reactive                | NA                           | NA                     | 127.8                 | 73.44                          | 79.84                          | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | corticosteroids                | Gl                              | Hodgkin lymphoma                |
| 4  | 67  | m   | HES                     | NA                           | NA                     | 0.88                  | 95.10                          | 82.28                          | NA                              | 100.93                         | NA                              | NA                              | NA                              | NA                              | NA                              | corticosteroids                | Gl                              | lung                            |
| 5  | 33  | f   | HES                     | 15                            | 1.0                    | 2.28                  | 98.20                          | 85.79                          | NA                              | 92.06                          | NA                              | NA                              | NA                              | NA                              | NA                              | corticosteroids                | Gl                              | skin                            |
| 6  | 49  | m   | HES                     | 24                            | 2.2                    | NA                     | 103.84                         | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | corticosteroids                | skin, PNS                       | Angioedema                      |
| 7  | 58  | f   | HES                     | 15                            | 0.8                    | NA                     | 107.20                         | 95.53                          | 77.81                          | 81.70                          | 17.06                          | 27.38                          | NA                              | 8.41                            | none                            | skin, lung, kidney              | Mast cell proliferation in BM, but no mastocytosis |
| 8  | 28  | f   | HES                     | 9                             | 0.3                    | NA                     | 96.82                          | 87.79                          | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | fexofenadine                    | Mast cell proliferation in BM, but no mastocytosis |
| 9  | 76  | m   | HES                     | 8                             | 0.5                    | 1.52                  | 74.13                          | 94.44                          | NA                              | 92.40                          | NA                              | NA                              | NA                              | NA                              | NA                              | corticosteroids                | Gl, lung, kidney                | Angioedema                      |
| 10 | 36  | m   | HES                     | 38                            | 5.7                    | 0.89                  | 91.36                          | 104.39                         | NA                              | 70.74                          | 98.40                          | 95.83                          | NA                              | 76.47                          | NA                              | heart                          | Mast cell proliferation in BM, but no mastocytosis |
| 11 | 33  | m   | HES                     | 39                            | 5.7                    | 2.94                  | 97.90                          | 100.00                         | NA                              | 97.79                          | 80.62                          | NA                              | NA                              | NA                              | NA                              | corticosteroids                | Gl, lung, kidney                | AKI                             |
| 12 | 49  | m   | HES                     | 29                            | 1.8                    | 0.85                  | 101.29                         | 88.49                          | 71.93                          | 68.05                          | 104.72                         | 112.18                         | 114.73                         | NA                              | corticosteroids                | kidney                          | Thrombocytopenia                |
| 13 | 62  | f   | HES                     | NA                            | NA                     | 1.43                  | 82.34                          | 56.93                          | 41.17                          | 75.82                          | NA                              | NA                              | NA                              | NA                              | NA                              | corticosteroids                | heart                          |
| 14 | 62  | m   | HES                     | 67                            | 15.8                   | 2.48                  | 98.07                          | 91.93                          | 87.23                          | 73.73                          | NA                              | NA                              | NA                              | NA                              | NA                              | allergy, Gl, lung              |
| 15 | 57  | f   | HES                     | 35                            | 2.6                    | 1.60                  | 98.29                          | 79.46                          | 72.49                          | 64.06                          | 92.34                          | 56.96                          | 103.01                         | 80.57                          | none                            | allergy, heart, ENT, lung       |
| 16 | 62  | m   | HES                     | 49                            | 6.2                    | 1.35                  | 86.96                          | 86.61                          | 92.00                          | 89.04                          | NA                              | NA                              | NA                              | NA                              | NA                              | corticosteroids, etanercept, adalimumab | Gl, lung, PNS                  | Primary sclerosing cholangitis |
| 17 | 35  | m   | HES                     | NA                            | NA                     | 1.41                  | 86.67                          | 20.54                          | 22.35                          | 14.20                          | 99.29                          | 96.33                          | 97.79                          | 62.25                          | corticosteroids                | skin                            |
| 18 | 35  | m   | HES                     | NA                            | NA                     | 161.16               | 69.01                          | 83.47                          | 72.31                          | 116.70                         | 86.99                          | 86.80                          | 52.62                          | NA                              | corticosteroids                | skin                            |
| 19 | 68  | f   | HES                     | NA                            | NA                     | 81.01                | 65.50                          | NA                              | 85.20                          | 84.48                          | NA                              | NA                              | NA                              | NA                              | NA                              | corticosteroids                | Gl                              |
| 20 | 47  | m   | HES                     | 8                             | 0.4                    | 1.31                  | 99.20                          | 92.24                          | 84.25                          | 86.19                          | NA                              | NA                              | NA                              | NA                              | NA                              | allergy, skin, lung             |
| 21 | 54  | m   | HES                     | 35                            | 2.6                    | 1.62                  | 98.15                          | 95.49                          | NA                              | 0.21                           | 100.34                         | 100.79                         | 95.48                          | none                            | heart                          |
| 22 | 40  | f   | L-HES                   | NA                            | NA                     | 1.72                  | 186.05                         | 66.28                          | 46.51                          | 150.00                         | NA                              | NA                              | NA                              | NA                              | NA                              | none                            |
| 23 | 69  | f   | L-HES                   | 18                            | 1.9                    | 2.97                  | 93.50                          | 57.23                          | 48.84                          | 94.65                          | NA                              | NA                              | NA                              | NA                              | R-CHOP                         | allergy                        |
| 24 | 78  | f   | MLN-Eo                  | 60                            | 8.0                    | 1.73                  | 86.07                          | 54.11                          | NA                              | 56.39                          | NA                              | NA                              | NA                              | NA                              | corticosteroids                | Gl                              | RIP111-POGFR A +                |
| 25 | 56  | m   | MLN-Eo                  | NA                            | NA                     | NA                     | NA                              | NA                              | NA                              | NA                              | 97.78                          | 84.71                          | 91.86                          | 42.54                          | NA                              | corticosteroids                | Gl                              | Anemia, thrombocytopenia, splenomegaly, RIP1- POGFR A + |
| 26 | 57  | m   | CEL-NDS                 | 34                            | 4.5                    | NA                     | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | corticosteroids                | heart                          | DNM/MTA mutation                |
| 27 | 70  | f   | CEL-NDS                 | 90                            | 68.0                   | 3.88                  | 78.41                          | 25.31                          | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | hydroxyurea                    | NA                              | <5% blasts in BM                |
| No. | Age | Gender | Diagnosis | WBC (x10^3/mm³) | MCH (pg) | MCV (fl) | MCHC (%) | Hematocrit (%) | Platelets (x10^3/μL) | Corticosteroids | ANCA | JAK2-V617F | Other
|-----|-----|--------|------------|-----------------|----------|---------|---------|---------------|-----------------|----------------|------|------------|--------|
| 28  | 80  | m      | CEL-NOS    | 28              | 7.4      | 1.44    | 102.24  | 88.04         | 60.90           | NA              | NA              |      |           |        |
| 29  | 62  | m      | CEL-NOS    | NA              | NA       | NA      | 111.75  | 94.61         | 85.56           | 60.71           | NA              |      |            | corticosteroids |
| 30  | 67  | m      | CEL-NOS    | 27              | 2.5      | 0.83    | 99.78   | 97.67         | 99.45           | 96.89           | 96.58           | 95.29 | 97.43      | 63.42      |
| 31  | 62  | f      | CEL-NOS    | NA              | NA       | NA      | 100.68  | 83.13         | 76.87           | 62.86           | 95.77           | 92.86 | 97.89      | 64.79      |
| 32  | 82  | m      | CEL-NOS    | 40              | 10.0     | 1.41    | 88.51   | 36.66         | 69.09           | 13.92           | 83.97           | 23.71 | 81.80      | none       |
| 33  | 62  | m      | CEL-NOS    | 6               | 0.6      | 0.93    | 96.93   | 63.45         | 41.08           | 96.49           | NA              | NA              | NA          | corticosteroids |
| 34  | 75  | f      | CEL-NOS    | 80              | 32       | NA      | 100.88  | 85.29         | 81.87           | 95.24           | 60.96           | 25.31 | 29.06      | 48.31      |
| 35  | 65  | f      | EGPA       | 36              | 3.9      | 2.42    | 102.41  | 89.26         | 78.77           | 20.14           | NA              | NA              | NA          | rituximab    |
| 36  | 49  | f      | EGPA       | 17              | 1.7      | 1.86    | 207.09  | 167.72        | 161.42          | 170.08          | NA              | NA              | NA          | IVIG        |
| 37  | 82  | f      | EGPA       | 7               | 0.5      | NA      | NA      | NA            | NA              | NA              | NA              | NA          | mepolizumab |
| 38  | 48  | f      | EGPA       | 28              | 1.5      | NA      | NA      | NA            | NA              | NA              | NA              | NA          | ENT            |
| 39  | 55  | f      | EGPA       | 16              | 1.4      | NA      | 97.52   | 97.88         | NA              | 87.60           | NA              | NA              | corticosteroids |
| 40  | 43  | f      | EGPA       | 52              | 11.5     | 4.42    | 99.13   | 85.22         | NA              | 130.00          | 68.22           | 62.29           | NA          | corticosteroids |
| 41  | 47  | m      | EGPA       | 8               | 0.4      | 1.41    | 109.06  | 99.61         | 92.76           | 87.06           | NA              | NA              | NA          | ENT            |
| 42  | 66  | f      | EGPA       | NA              | NA       | 1.33    | 57.36   | 47.36         | 70.38           | 15.38           | NA              | NA              | NA          | mepolizumab |
| 43  | 78  | f      | EGPA       | 24              | 3.1      | 0.47    | 104.76  | 89.09         | 70.07           | 41.54           | NA              | NA              | NA          | ent          |
| 44  | 77  | m      | EGPA       | 35              | 6.0      | 2.12    | 92.16   | 87.16         | 73.92           | 7.85            | NA              | NA              | NA          | corticosteroids |
| 45  | 57  | f      | EGPA       | 66              | 19.8     | NA      | 98.74   | 90.77         | 90.77           | 82.55           | 72.43           | 65.65 | 63.08      | 81.54      |

**Notes:**
- ANCA: Anti-neutrophil cytoplasmic antibodies
- JAK2 p.T556V asoc mutation
- 5-10% blasts in BM
- TET2, JAK2 V617F mutations
- allergy, ENT, lung, PNS
- skin, heart, ENT, lung, kidney
- skin, lung, kidney, PNS
- ANCA negative
**Supplementary Table 2:**

Gene expression of critical BCL-2 family members in primary human eosinophils of hypereosinophilic patients contributing samples. Age, sex, WHO category and gene expression levels were documented for each patient sample. Gene expression levels are expressed as fold change. Criteria for hypereosinophilia and hypereosinophilic syndromes were applied as defined in the WHO Update 2019.  

$m =$ male,  
$f =$ female,  
HES =$ hypereosinophilic syndrome,  
L-HES =$ lymphocyte variant hypereosinophilic syndrome,  
MLN-Eo =$ eosinophilia-associated myeloproliferative neoplasia,  
CEL-NOS =$ chronic eosinophilic leukemia not otherwise specified,  
EGPA =$ eosinophilic granulomatosis with polyangiitis,  
NA $=$ not available.
| ID | Age | Sex | Type of Hyperesinophilis | BCL-2 | BCL-xL | MCL1 | BIM | MORRBID | BCL-w | PUMA | NOXA | BAK | BAX |
|----|-----|-----|--------------------------|-------|--------|------|-----|--------|-------|------|------|-----|-----|
| 1  | 66  | m   | reactive                 | NA    | NA     | NA   | NA  | NA     | NA    | NA   | NA   | NA  |     |
| 2  | 60  | f   | reactive                 | NA    | NA     | NA   | NA  | NA     | NA    | NA   | NA   | NA  |     |
| 3  | 27  | f   | reactive                 | NA    | NA     | NA   | NA  | NA     | NA    | NA   | NA   | NA  |     |
| 4  | 67  | m   | HES                      | NA    | NA     | NA   | NA  | NA     | NA    | NA   | NA   | NA  |     |
| 5  | 33  | f   | HES                      | NA    | NA     | NA   | NA  | NA     | NA    | NA   | NA   | NA  |     |
| 6  | 49  | m   | HES                      | NA    | NA     | NA   | NA  | NA     | NA    | NA   | NA   | NA  |     |
| 7  | 58  | f   | HES                      | NA    | NA     | NA   | NA  | NA     | NA    | NA   | NA   | NA  |     |
| 8  | 28  | f   | HES                      | NA    | NA     | NA   | NA  | NA     | NA    | NA   | NA   | NA  |     |
| 9  | 76  | m   | HES                      | NA    | NA     | NA   | NA  | 7,808  | 8,486 | 0,226| 0,115| 0,023| 36,631|0,003|
| 10 | 36  | m   | HES                      | 1,602 | 6,042  | 9,781| 3,138| 2,621  | 0,250 | NA   | 0,646| 10,267|5,063|
| 11 | 33  | m   | HES                      | 2,362 | 9,158  | 19,973| 5,205| 6,000  | 0,157 | 0,074| 2,071| 7,362|0,006|
| 12 | 49  | m   | HES                      | NA    | NA     | 3,227| 9,646| 2,129  | NA    | NA   | 4,000| NA   | 5,676|
| 13 | 62  | f   | HES                      | 4,724 | 6,169  | 23,103| 4,317| 3,904  | 0,255 | 0,162| 2,657| 7,111|NA   |
| 14 | 62  | m   | HES                      | 0,624 | 58,485 | 69,792| 8,056| 31,017 | 0,664 | 1,025| NA   | 62,250|NA   |
| 15 | 57  | f   | HES                      | 2,612 | 2,898  | 11,432| 3,387| 5,796  | 0,032 | 0,167| 3,706| 5,676|0,019|
| 16 | 62  | m   | HES                      | 0,032 | NA     | NA   | 17,268| 9,580  | NA   | NA   | 24,420|23,183|NA   |
| 17 | 35  | m   | HES                      | 2,107 | 1,905  | 88,035| 16,564| 3,317  | 0,120 | NA   | 5,502| 9,580|0,011|
| 18 | 35  | m   | HES                      | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 19 | 68  | f   | HES                      | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 20 | 47  | m   | HES                      | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 21 | 54  | m   | HES                      | NA    | NA     | NA   | NA   | 6,521  | NA    | NA   | 33,014|NA   |     |
| 22 | 40  | f   | L-HES                    | NA    | 2,035  | NA   | 258,676| 32,900| 0,050| NA   | 73,772|NA   |     |
| 23 | 69  | f   | L-HES                    | 0,022 | 11,794 | NA   | 36,886| 17,030 | 0,046| NA   | 0,039| 4,485|0,460|
| 24 | 78  | f   | MLN-Eo                   | NA    | NA     | NA   | 56,886| 9,747  | NA   | NA   | 102,893|0,206|
| 25 | 56  | m   | MLN-Eo                   | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 26 | 57  | m   | CEL-NOS                  | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 27 | 70  | f   | CEL-NOS                  | NA    | NA     | NA   | 6,566| 10,021 | NA    | NA   | 0,232| NA   | 4,408|
| 28 | 80  | m   | CEL-NOS                  | NA    | NA     | NA   | 7,674| 1,197  | NA    | NA   | 110,278|NA   |     |
| 29 | 62  | m   | CEL-NOS                  | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 30 | 67  | m   | CEL-NOS                  | 5,676 | 13,132 | 38,720| 17,448| 11,672 | 0,172 | 24,001| 14,320|8,427|
| 31 | 62  | f   | CEL-NOS                  | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 32 | 82  | m   | CEL-NOS                  | 2,732 | 23,835 | 109,516| 19,093| 9,158  | 0,536 | 1,068| NA   | 35,261|11,392|
| 33 | 62  | m   | CEL-NOS                  | 1,329 | 9,000  | 12,084| 17,630| 5,315  | 0,209| NA   | 0,055| 2,049|2,576|
| 34 | 75  | f   | CEL-NOS                  | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 35 | 65  | f   | EGPA                     | NA    | 0,241  | 1,003| 4,579| 3,238  | NA    | NA   | 0,018| 11,592|0,001|
| 36 | 49  | f   | EGPA                     | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 37 | 82  | f   | EGPA                     | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 38 | 48  | f   | EGPA                     | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 39 | 55  | f   | EGPA                     | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 40 | 43  | f   | EGPA                     | 9,190 | 6,364  | 25,546| 5,389| 6,212  | 0,361| 0,776| 1,197| 9,747|4,213|
| 41 | 47  | m   | EGPA                     | NA    | NA     | NA   | 0,946| 1,840  | 0,019| NA   | NA   | 0,993|NA   |
| 42 | 66  | f   | EGPA                     | 1,952 | 7,285  | 14,123| 12,597| 9,646  | 0,062| 1,873| 0,030| 11,794|NA   |
| 43 | 78  | f   | EGPA                     | NA    | NA     | NA   | 0,455| 8,427  | 6,751 | NA   | NA   | 1,083|NA   |
| 44 | 77  | m   | EGPA                     | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
| 45 | 57  | f   | EGPA                     | NA    | NA     | NA   | NA   | NA     | NA    | NA   | NA   | NA   |NA   |
**Supplementary Table 3:**
Following primer sequences were used for RT-qPCR analysis as described in Material and Methods.

| Target RNA   | Primer sequence                                      |
|--------------|------------------------------------------------------|
| **HPRT**     | 5' - GCT ATA AAT TCT TTG CTG ACC TGC TG - 3'
               | 5' - AAT TAC TTT TAT GTC CCC TGT TGA CTG G - 3' |
| **BCL2L11 (BIM)** | 5' - GGT CCT CCA GTG GGT ATT TCT CTT - 3'
               | 5' - ACT GAG ATA GTG GTT GAA GGC CTG G - 3' |
| **BCL-2**    | 5' - GAT AAC GGA GGC TGG GAT G - 3'
               | 5' - TCA CTT GTG GCC CAG ATA GG - 3' |
| **MCL1**     | 5' - AGA AAG CTG CAT CGA ACC AT - 3'
               | 5' - CCA GCT CCT ACT CCA GCA AC - 3' |
| **BCL-xL**   | 5' - CTT GGA TGG CCA CTT ACC TG - 3'
               | 5' - AAG AGT GAG CCC AGC AGA AC - 3' |
| **BCL-w**    | 5' - GGA CAA GTG CAG GAG TGG AT - 3'
               | 5' - GTC CTC ACT GAT GCC CAG TT - 3' |
| **BAK**      | 5' - ACC AGC CTG TTT GAG AGT GG - 3'
               | 5' - GGC CTA GGA AGC CAG TCA G - 3' |
| **BAX**      | 5' - TTT GCT TCA GGG TTT CAT CC - 3'
               | 5' - ATC CTC TGC AGC TCC ATG TT - 3' |
| **NOXA**     | 5' - AAG AAG GCG CGC AAG AAC - 3'
               | 5' - TCC TGA GCA GAA GAG TTT GGA - 3' |
| **PUMA**     | 5' - GGG GAG GAG GAA CAG TGG - 3'
               | 5' - AGG AGT CCC ATG ATG AGA TTG T - 3' |
| **MORRBID**  | 5' - ACT GGA TGG TCG CTG CTT TT - 3'
               | 5' - CTT CCC AGG AAC TGT GCT GT - 3' |