Statistical Analysis Plan

Protocol Title: Double-Blind, Randomized, Placebo-Controlled Trial of AKST4290 for Adjunctive Treatment of Mild to Moderate Bullous Pemphigoid

Protocol Number: AKST4290-221

Protocol Version number and date:	V4.0, 15May2020
SAP Version number and date:	V1.0, 10Aug2021
Sponsor:	Alkahest, Inc.
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2. Revision history

2.1. Summary of changes

Statistical Analysis Plan version 1.0 is the initial revision.

Changes from one approved revision to the next will be summarized in the table below.

Section	Description	Justification

3. Table of Contents

[redacted]

[redacted]

[redacted]

[redacted]

4. Abbreviations

AE(s)	Adverse Event(s)
AESI	Adverse Events of Special Interest
ATC	Anatomical Therapeutic Chemical
BP	Bullous Pemphigoid
b.i.d	Twice Daily
BPDAI	Bullous Pemphigoid Disease Area Index
BPDAI-VAS	Bullous Pemphigoid Disease Area Index Visual Analog Scale
CI	Confidence Interval
CL	Confidence Limit
CPC	Clobetasol Propionate Cream
DF	Degrees of Freedom
DLQI	Dermatology Life Quality Index
ECG	Electrocardiogram
[redacted]	[redacted]
eCRF	Electronic Case Report Form
FAS	Full Analysis Set
GCP	Good Clinical Practice
IFN-g	Interferon gamma
IgG	Immunoglobulin G
IL	Interleukin
MFC	Mometasone Furoate Cream
MoCA	Montreal Cognitive Assessment
PK	Pharmacokinetic(s)
PT	Preferred Term
SAE(s)	Serious Adverse Event(s)
SAP	Statistical Analysis Plan
SAR	Statistical Analysis Report
SD	Standard Deviation

SDTM	Study Data Tabulation Model
SE	Standard Error
SOC	System Organ Class
VAS	Visual Analog Scale
WHO	World Health Organization

5. Definitions

Adverse event surveillance period (for a subject)	Adverse events (AEs) are recorded from the time of informed consent. All AEs that occur after the first dose of study drug will be considered Treatment Emergent AEs. Subjects with Treatment Emergent AEs must be followed until the AE is resolved or is stable, unless the subject is lost to follow up.
Baseline	Visit 2 (day 1). If a measurement is performed during Visit 1 (Screening), but not Visit 2, then the measurement performed at Visit 1 is considered the baseline measurement.
BPDAI score	Either the total BPDAI activity score or the total BPDAI damage score. Both the activity score and the damage score are the arithmetic sums of their components (see Protocol section 7.1.1.3.1). For the activity score, each item in each of the lists Skin Erosions/Blisters, Skin Urticaria/Erythema/Other and Mucosa Erosion/Blisters is graded from 0 to 10 (see Protocol section 17.1 for the items and possible grades), and all items' grades are summed. The score reported in the eCRF question "Total BPDAI Activity Score" is used for analyses. For the damage score, each item in the Skin list is graded with 0 or 1 (see Protocol section 17.1 for the items), and the grades summed. The score reported in the eCRF question "Total BPDAI Damage Score" is used for analyses.
BPDAI-VAS score	The intensity of pruritus is assessed using a visual analog scale to answer the question, ''How severe is your itching today?'' and the subject marks an ''x'' on the 0- to 10-cm line where 0 is no itch and 10 is maximal itching. The degree of itching is measured as the distance in centimeters from 0, out of 10. This is repeated for the severity overall of itching in the past week and month. A total score is calculated from this out of 30 (see Protocol Section 17.2 for the items).
Incidence (of an event, among a group)	Proportion of subjects experiencing at least one event of the specified kind.
Time to disease control	Number of days from randomization to date of disease control as recorded on the eCRF.
Time to rescue therapy	Number of days from randomization to date of initial dose of rescue therapy as recorded on the eCRF.
Treatment group	Either AKST4290 or placebo.

6. Protocol summary

This is a randomized, double-blind, placebo-controlled phase 2 trial to be conducted at up to 8 sites in approximately 30 subjects to assess the therapeutic effect and safety of adjunctive AKST4290 in subjects with mild to moderate bullous pemphigoid (BP). Subjects will receive whole-body topical mometasone furoate cream (MFC) therapy (dose and dosing interval dependent upon severity of disease at time of enrollment, as assessed by the investigator) concurrently with the study agent (placebo or AKST4290 400 mg twice daily (b.i.d)) in an inpatient setting until disease control is reached (duration of inpatient stay is dependent upon individual disease course – estimated between 1–3 weeks). Study agent dosing will commence once eligibility has been confirmed and may start up to 7 days after the start of whole-body topical steroid therapy. Following clinical diagnosis, histological diagnosis of BP will subsequently be confirmed per the S2k Guideline for the Diagnosis of Pemphigus Vulgaris/Foliaceus and Bullous Pemphigoid (Schmidt 2015). Subjects will receive rescue therapy at any time if their clinical condition worsens or if their clinical condition fails to improve by the completion of Week 1 on study treatment, as assessed by the investigator. Rescue therapy will consist of whole body clobetasol propionate cream (CPC) (15-50g) and/or oral prednisone (0.5 mg/kg per day), as determined by the investigator. Subjects who receive rescue therapy will remain in the study until disease control, unless they are withdrawn or withdraw from participation.

7. Study objectives

7.1. Primary objective

To investigate the proportion of subjects who achieve disease control (defined as ≤ 3 new blisters/eczematous lesions/urticarial plaques and healing of existing blisters/eczematous lesions/urticarial plaques) following topical steroid treatment with adjunctive AKST4290 without receiving rescue therapy.

7.2. Secondary objectives

To assess the safety of AKST4290. Additional secondary endpoints include assessment of time to disease control; time to rescue therapy; change in BP Disease Area Index (BPDAI) score; and change in pruritis as assessed by the BPDAI-Visual Analog Scale (BPDAI-VAS). In addition, change in skin (biopsy) [redacted] counts and overall steroid dose required to achieve disease control will be assessed.

7.3. Exploratory objectives

Blister fluid protein levels [redacted] counts, anti-BP180 Immunoglobulin G [IgG] serum levels, serum protein levels [redacted], and blood chemistry will be evaluated. Pharmacokinetic (PK) studies will also be conducted to assess AKST4290 plasma concentrations at various required and optional timepoints. Cognitive assessments will be performed using the Montreal Cognitive Assessment (MoCA). Quality of life will be assessed by the Dermatology Life Quality Index (DLQI). Additional biomarker evaluations may be conducted on plasma samples.

8. Study endpoints

8.1. Primary endpoint

The proportion of subjects who achieve disease control (defined as no more than (≤) 3 new blisters/eczematous lesions/urticarial plaques and healing of existing blisters/eczematous lesions/urticarial plaques) without requiring rescue therapy.

8.2. Secondary endpoints

1. Safety as assessed by the incidence, seriousness, and severity of adverse events (AEs).
2. Time to disease control by treatment day/week.
3. Time to rescue therapy by treatment day/week.
4. Change from baseline in BPDAI score by treatment week and at disease control.
5. Change from baseline in pruritus as evaluated by the BPDAI-VAS by treatment week and at disease control.
6. Change from baseline in skin biopsy [redacted] levels at disease control.
7. Evaluation of total cumulative steroid exposure at baseline, by treatment week and at disease control.
8. Evaluation of maximum daily steroid dose at baseline, by treatment week and at disease control.

8.3. Exploratory endpoints

1. Change from baseline in blister fluid protein levels [redacted] at treatment Week 1.
2. Change from baseline in blood [redacted] levels by treatment week and at disease control.
3. Change from baseline in Anti-BP180 IgG levels by treatment week and at disease control.
4. Evaluations of complete blood count (CBC), blood chemistry, and serum protein levels [redacted] at baseline, by treatment week and at disease control.
5. Changes in AKST4290 plasma concentrations at various timepoints.
6. Change from baseline in cognitive assessments using the MoCA at disease control.
7. Change from baseline in quality of life, as assessed by the DLQI at disease control.
8. Evaluation of exploratory biomarkers in plasma samples at various timepoints.

9. Sample size

A final sample size of 30 subjects was chosen based on clinical experience.

10. General considerations for data analysis

10.1. General principles

As detailed in the protocol, the sample size of 30 subjects was chosen based on clinical experience with the intent of obtaining 27 evaluable subjects. Due to the treatment limitations, rarity of the disease, coronavirus disease 2019 (COVID-19) pandemic and expiry of Investigational Medicinal Product (IMP), enrollment ended with a total of six subjects enrolled and completing the study. Due to the reduced number of enrolled subjects, analysis described in the SAP focuses on a descriptive summary of efficacy and safety within summary tables and figures and data primarily reported in listing format. Section 7 (Study Objectives) and Section 8 (Study Endpoints) of the SAP present the protocol-defined study objectives and endpoints; Section 11 (Summary of study population), Section 12 (Safety analyses) and Section 13 (Efficacy analyses) describe an abridged analytical plan relative to what was presented in the study protocol. The reduced set of planned analyses generally consists of descriptive summaries of essential study endpoints and is more appropriate given the smaller subject enrollment than was originally planned.

All summary statistics will be descriptive unless noted otherwise. Descriptive summaries will include the number of subjects (n), mean, standard deviation (SD) or standard error of the mean (SE), median, first quartile (Q1), third quartile (Q3), and range for continuous variables and number and percentages for categorical variables.

Subjects will be analyzed in the treatment group assigned at randomization for the ITT data sets. For the Safety Evaluable data set, subjects will be grouped according to actual treatment received.

10.2. Analysis datasets

10.2.1. Intent-to-Treat (ITT) Set

The full analysis set (FAS) includes the set of subjects that is as close as possible to the ideal implied by the Intention-to-treat principle. It is derived from the set of all randomized subjects by minimal and justified elimination of subjects.

10.2.2. Safety Evaluable Set

The Safety Evaluable set will include all randomized subjects who receive at least 1 dose of the study agent (placebo or AKST4290).

10.3. Data transformations and derivations

Values will be presented for all scheduled study visits according to the nominal visit obtained from the eCRF. If an unscheduled visit falls in a visit window with an existing nominal visit assessment, the nominal assessment will be used in analyses. If no nominal visit assessment exists for a visit window with unscheduled visit(s), then the first unscheduled visit within the visit window will be used.

If the End of Treatment visit is performed in place of a scheduled weekly visit, the measurements of the End of Treatment visit are also used for that scheduled weekly visit. This is assumed to be the case if the End of Treatment visit falls into the protocol-specified visit window of some scheduled visit, and that particular scheduled visit is not done.

All heights will be converted to centimeters, all weights to kilograms, and all temperatures to Celsius units.

10.4. Missing data and imputation

No explicit imputation will be used.

All partial dates will be identified, and partial dates will be imputed as follows:

- If day and month are missing but year is available, then the imputed day and month will be 01 Jan;
- If day is missing and month and year are available, then the imputed day will be the first day of the month;
- A partial date will not be imputed if the year is missing.

10.5. Sub-groups

Analysis of disease control will include a stratified assessment of whether or not subjects reach disease control by subjects who enroll with/without fulfilling all of the eligibility criteria. Further details are provided in Section 13.1.

10.6. Covariates

No covariates will be included in the primary analyses.

10.7. Multicenter studies

The main analyses will not be adjusted for study center.

10.8. Multiple comparisons

No adjustments for multiplicity will be employed. Multiple testing issue is acknowledged for the numerous treatment group comparisons in safety analyses (one comparison for each type of AE, each laboratory parameter etc.), but nothing will be explicitly adjusted.

10.9. Timing of analyses

The final analysis will be performed after the database is locked. However, statistical programming for the final analysis based on blinded (mock) data will commence before database lock.

10.10. Interim analyses

There is no planned interim analysis for this study.

10.11. Software

Data analyses will be performed with SAS® version 9.4 or higher.

10.12. Reporting conventions

10.12.1. General

Range or min, max values will be rounded to the precision of the original value, means, and medians will be rounded to 1 decimal place greater than the precision of the original value, and SDs or SEs will be rounded to 2 decimal places greater than the precision of the original value. Percentages will generally be rounded to the nearest whole number (trailing decimal zeroes are not displayed).

10.12.2. Tables

All summary tables will be structured with a column for each treatment group, unless treatment group is clearly irrelevant for the summary (e.g., reasons for screening failures). All summary tables will be annotated with the analysis set and total population size relevant to that table. Mock tables are included in section 18.

10.12.3. Listings

Listings will generally present the data as it appears on the eCRFs without any further grouping or pooling as used in the analyses. In general, a listing will be developed for each eCRF utilized in the study; any derived values used in table or figure analysis will be reported at the subject level in the associated listing.

Listings will be formatted as separate Excel files. Most listings will not be included in the main body of the Statistical Analysis Report (SAR), except for (at least) the listings of serious adverse events and adverse events of special interest.

Any listings that are "by subject" have all the results of one subject in one row, with a space reported between each subject entry. Any listings that are "by subject by visit" have one row per subject per visit. Otherwise, different results of one subject may be organized to separate rows in some other way (e.g., one medical history element per row). Listings that include multiple rows per subject will only report the first occurrence of repeat variables in the data presentation. If possible, all entries for a subject will be maintained on the same page and will only split entries between pages if necessary due to space limitations. All listings are sorted by the site, subject number and treatment group.

11. Summary of study population

11.1. Subject disposition

Subject disposition will be presented for the ITT set. Summaries will include the number and percentage of subjects also in the Safety Evaluable set, completing the study, and discontinuing early by the reason for discontinuation by treatment group and over all subjects combined.

11.2. Demographic and other baseline characteristics

Demographics and baseline characteristics will include descriptive statistics of age, race, gender, height (cm), weight (kg), ethnicity, educational level, severity of BP (mild or moderate), total BPDAI activity score, total BPDAI skin blister score and total BPDAI skin urticarial score, total BPDAI mucosal activity score, total BPDAI damage score, total BPDAI-VAS score. Age will be calculated relative to the date of informed consent using birth year from the CRF. Each of these variables will be summarized by treatment group and over all subjects combined for the ITT population.

11.3. Medical history

Medical history elements will be coded to a Preferred Term (PT) and a System Organ Class (SOC) using the Medical Dictionary for Regulatory Activities (MedDRA). Medical History will be presented in a listing to include concomitancy (resolved or ongoing).

11.4. Prior and concomitant medications

Prior and Concomitant medication data will be collected throughout the study on the Prior and Concomitant Medications eCRF page. The start and stop dates for each medication will be compared to

the **date of randomization** to allow them to be classified as prior and concomitant. Prior medications are medications with start and stop dates prior to the date of randomization. Other medications are considered concomitant.

If medication start and/or stop dates are missing or partial, the dates will be compared as far as possible with the date of randomization. Medications will be assumed to be concomitant, unless there is clear evidence (through comparison of partial dates) to suggest that the medication stopped prior to the date of randomization. If there is clear evidence to suggest that the medication stopped prior to randomization, the medication will be assumed to be prior.

Medications will be coded with the World Health Organization (WHO) drug dictionary and mapped to Anatomic Therapeutic Chemical (ATC) drug class (level 1) and drug name. Prior and concomitant medications will be presented in a listing to include all medications by generic name and verbatim name.

Prior topical steroid treatment will be collected on the Steroid Treatment eCRF. Data as reported on the CRF will be presented in a listing.

11.5. Treatment compliance

As the study agent is administered under direct supervision of the study staff, no problems with treatment compliance are anticipated. Therefore, treatment compliance will not be analyzed separately; study drug administration will be presented in a listing.

11.6. Protocol deviations

Subject-specific protocol deviations will be summarized in a listing to include category (minor, major) and type (GCP, protocol). Categories of protocol deviations are defined in the Protocol Deviation Plan (see study protocol section 13.3).

12. Safety analyses

The Safety Evaluable Analysis Set will be used for all analyses and tables of safety data.

12.1. Adverse events

All subjects who have given informed consent will be evaluated for AEs. AEs will be reviewed, documented, and reported as required at each visit, beginning at screening. All AEs that occur after the time of treatment with the study drug will be considered Treatment Emergent AEs. All reported terms (investigator descriptions) for AEs will be encoded according to the Medical Dictionary for Regulatory Activities (MedDRA). As SAE is a type of AE, all analyses of AEs will also include SAEs.

Summaries that are displayed by system organ class and preferred terms will be ordered by descending incidence of system organ class and preferred term within each system organ class. Summaries of the following types will be presented:

- Overall summary of number of unique TEAEs and treatment-emergent SAEs and subject incidence of TEAEs meeting various criteria;
- Subject incidence of TEAEs by MedDRA system organ class and preferred term;
- Subject incidence of TEAEs by relationship to study drug, MedDRA system organ class, and preferred term

At each level of summarization (eg, any AE, system organ class, and preferred term), subjects experiencing more than one TEAE will be counted only once. In the summary of TEAEs by severity grade, subjects will be counted once at the highest severity reported at each level of summarization; in the summary of TEAEs by relationship, subjects will be counted once at the closest relationship to study drug.

Adverse event data will be presented in data listings by subject, treatment group, and event. All deaths during the study will be listed by subject, to include the primary cause of death. Serious AEs and AEs leading to discontinuation of the study drug will be presented in separate data listings. A listing of AEs that qualify as adverse of special interest (AESI) will also be reported; per protocol, an AESI includes events of:

- [redacted]

12.2. Laboratory evaluations

For each laboratory test (hematology, chemistry, coagulation, screening serology, and urinalysis), the parameters will be presented in data listings by subject, treatment group, and collection date. Normality interpretation (Normal, High, Low, Panic High, Panic Low) will be obtained from the Clinical Status assessment from the central lab (see Data Transfer Plan section 14 – EDF-Format). Laboratory measurements identified as abnormal for hematology, chemistry and coagulation will be presented separately by subject, laboratory test, and unit in individual data listings.

12.3. Vital signs

Results of vital sign measurements will be presented in a data listing.

12.4. Physical examination

Results of the physical examination and targeted physical examination will be presented in a data listing.

12.5. 12-lead ECG

Results of the 12-lead ECG will be presented in a data listing.

12.6. Pregnancies

No pregnancies are expected to occur during the study. If any, these will be listed without any quantitative analysis.

13. Efficacy analyses

The ITT set will be used for the main analyses of efficacy. Efficacy summaries will focus on descriptive summaries of essential study endpoints.

13.1. Disease control without rescue therapy

The number and percent of subjects who did or did not experience disease control will be presented by treatment group; additionally, the number and percent of subjects who achieved disease control without the need for rescue therapy as well as the number and percent of subjects who required rescue therapy

will be reported by treatment group. The same analysis will be assessed stratifying by those subjects who fulfilled all eligibility criteria and those who did not as determined by the Inclusion/Exclusion criteria CRF. Listings will be included that present the daily SOC disease assessments used to determine disease control as well as the disease control and rescue therapy classifications for each subject.

13.2. Time to disease control

According to the study protocol, disease control is evaluated on a daily basis as part of Standard of Care, and the date of disease control is explicitly recorded in the eCRF.

For subjects who achieve disease control, the time to disease control will be calculated as:

$$\text{Time to disease control (days)} = \text{Date of disease control} - \text{Date of Visit 2 (Baseline (Day 1))} + 1$$

In cases of **study discontinuation** for whatever reason before achieving disease control, or those who do not experience disease control and reach end of study, subjects will be censored at their date of study completion/discontinuation. The time to disease control is calculated as:

$$\text{Time to disease control (days)} = \text{Date of study completion/discontinuation} - \text{Date of Visit 2 (Baseline (Day 1))} + 1$$

Time to disease control will be presented in a listing.

13.3. Time to Rescue therapy

Time to rescue therapy will be defined as the time to the start date of the first reported administration of steroid treatment, per the Steroid Treatment CRF, that is reported as "Rescue" for the Timing of Use variable.

For subjects who **will be positively assessed for the need of rescue therapy**, the time to rescue therapy will be calculated as:

$$\text{Time to rescue therapy (days)} = \text{Start date of first rescue treatment} - \text{Date of Visit 2 (Baseline (Day 1))} + 1$$

In cases of **study discontinuation or a subject completing study without the need for rescue therapy**, the time will be calculated as follows:

$$\text{Time to rescue therapy (days)} = \text{Date of study completion/discontinuation} - \text{Date of Visit 2 (Baseline (Day 1))} + 1$$

Time to rescue therapy will be presented in a listing.

13.4. BP Disease Area Index

Observed values and change from baseline in total BPDAI activity score, BPDAI activity subscales, and total BPDAI damage score at End of Treatment (EOT)/disease control will be summarized between treatment groups using descriptive statistics. The change from baseline summarization at EOT will include the EOT assessment reported for ITT subjects. The summary at disease control will include the EOT visit results from subjects who achieved disease control during Weeks 1-3.

Both the activity score and the damage score are the arithmetic sums of their components (see Protocol section 7.1.1.3.1). For the activity score, each item in each of the lists Skin Erosions/Blisters, Skin

Urticaria/Erythema/Other and Mucosa Erosion/Blisters is graded from 0 to 10 (see Protocol section 17.1 for the items and possible grades), and all items' grades are summed. The score reported in the eCRF question "Total BPDAI Activity Score" is used for analyses. For the damage score, each item in the Skin list is graded with 0 or 1 (see Protocol section 17.1 for the items), and the grades summed. The score reported in the eCRF question "Total BPDAI Damage Score" is used for analyses.

Total BPDAI activity score, total BPDAI damager score, the subscales used to calculate the total BPDAI activity score and total BPDAI damage score (as well as change from baseline in these values) will be provided in a listing; the individual assessments collected on the CRF for BPDAI will also be presented in the listing.

13.5. Pruritus

Change from baseline in total BPDAI-VAS score will be summarized in the same manner as the total BPDAI activity score. Observed values and mean change from baseline is calculated by treatment group and summarized at each visit where parameters were scheduled to be collected using descriptive statistics. Analysis at Visit 5 (Week 3) will include those subjects who reach Week 3 without early termination or reaching disease control; EOT is summarized collectively in a separate analysis visit. A figure plotting subject level change from baseline in total BPDAI-VAS score will be reported for each post-baseline time point where BPDAI-VAS is scheduled to be collected per the clinical study protocol. A plot presenting change from baseline in BPDAI-VAS total scores at each post-baseline time point will also be provided by treatment group. A listing of the total BPDAI-VAS score, change from baseline in total BPDAI-VAS score, as well as the individual questions used to calculate the score, will also be provided.

13.6. Skin (biopsy) [redacted] count

Skin (biopsy) [redacted] counts are collected during skin biopsy at screening and at disease control (optional – only if blisters are present). Observed values and change from baseline in skin biopsy [redacted] levels at disease control will be summarized by treatment group using descriptive statistics. A data listing of individual skin [redacted] levels will be reported.

13.7. Steroid exposure

Descriptive statistics for total cumulative steroid exposure (cortisol equivalent/kg) will be summarized by treatment group. Steroid treatments will be standardized for their respective cortisol equivalent unit. To determine per kg exposure, the last subject weight reported prior to the initiation of steroid treatment (as reported by the start date) will be used. Total cumulative exposure will require assessment of the start and end date for each respective steroid treatment, in addition to the frequency reported for the treatment. Subjects that report a frequency of AS NEEDED, UNKNOWN, OTHER or INTERMITTENT will be discussed with the sponsor to determine the appropriate calculation.

A figure plotting the individual steroid exposure (cortisol equivalent/kg) per study day per subject will be presented. Steroid exposure per study day will be determined by an assessment of the start and stop dates reported for each steroid treatment on the Steroid Treatment CRF in combination with the frequency reported; daily exposure will distribute the dosing frequency evenly across the date range defined by the start and stop date for each treatment. A figure presented daily steroid exposure (cortisol equivalent/kg) will also be presented by treatment group. A listing of all steroid treatment administration will also be provided.

13.8. Serum protein levels and serum Anti-BP180 IgG

For each serum anti-BP180 igG, CBC, and serum protein levels [redacted] results will be reported in a listing.

13.9. Blister fluid protein levels

For each blister fluid protein level [redacted] results will be reported in a listing.

13.10. Biomarkers in plasma samples

Analysis of biomarkers in plasma samples is not included in this SAP and will be defined in a separate Exploratory Analysis Plan.

13.11. Cognitive assessments

The Montreal Cognitive Assessment total score, as well as the components used to derive the total score, will be presented in a listing.

13.12. Quality of life

The Dermatology Life Quality index score, as well as the components used to derive the score, will be presented in a listing.

14. Pharmacokinetic analyses

Only data from the AKST4290 group will be used for pharmacokinetic analyses.

Data handling methods outlined in study protocol section 17.9.4 will be followed (missing data not included, values below lower limit of quantification replaced with zero, parameter estimates and descriptive statistics only reported when at least 2/3 data are available).

AKST4290 concentration values will be reported in a figure, table and listing by analysis time point.

15. Changes to Methods Planned in the Protocol

As detailed in the protocol, the goal was to enroll a total of approximately 30 subjects with the aim of obtaining 27 evaluable subjects. Due to the treatment limitations, rarity of the disease, coronavirus disease 2019 (COVID-19) pandemic, and expiry of Investigational Medicinal Product (IMP), enrollment ended with a total 6 subjects.

Section 10.3 (Analysis Datasets) of the clinical study protocol includes a Per Protocol (PP) analysis set defined as “a subset of ITT subjects.” This analysis set will not be utilized in the statistical analysis due to the limited enrollment noted previously and the restriction to descriptive analysis of study endpoints.

Section 10.4 (Descriptions of Statistical Methods) of the clinical study protocol outlines analysis of the primary endpoint (Section 10.4.2), secondary endpoints (Section 10.4.3) and exploratory analysis (Section 10.4.6). Due to the limited enrollment in the study, the analysis defined in Section 11 (Summary of study population), Section 12 (Safety analyses), 13 (Efficacy analyses) and 14 (Pharmacokinetic analyses) of the SAP will be utilized.

16. Top-Line Data Presentation

The following assessments associated with the study endpoints, as reported by listings, tables, and figures (where applicable), will be provided as top-line results:

- Disease Control and Rescue Therapy
- BPDAI and BPDAI-VAS
- Adverse events
- Skin biopsy [redacted] levels
- Steroid exposure
- Blood [redacted] levels

17. References

Schmidt E, Goebeler M, Hertl M, Sárdy M, Sitaru C, Eming R, et al. S2k guideline for the diagnosis of pemphigus vulgaris/foliaceus and bullous pemphigoid. J Dfsch Dermatol Ges. 2015;13(7):713-727.

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14.2 Efficacy data

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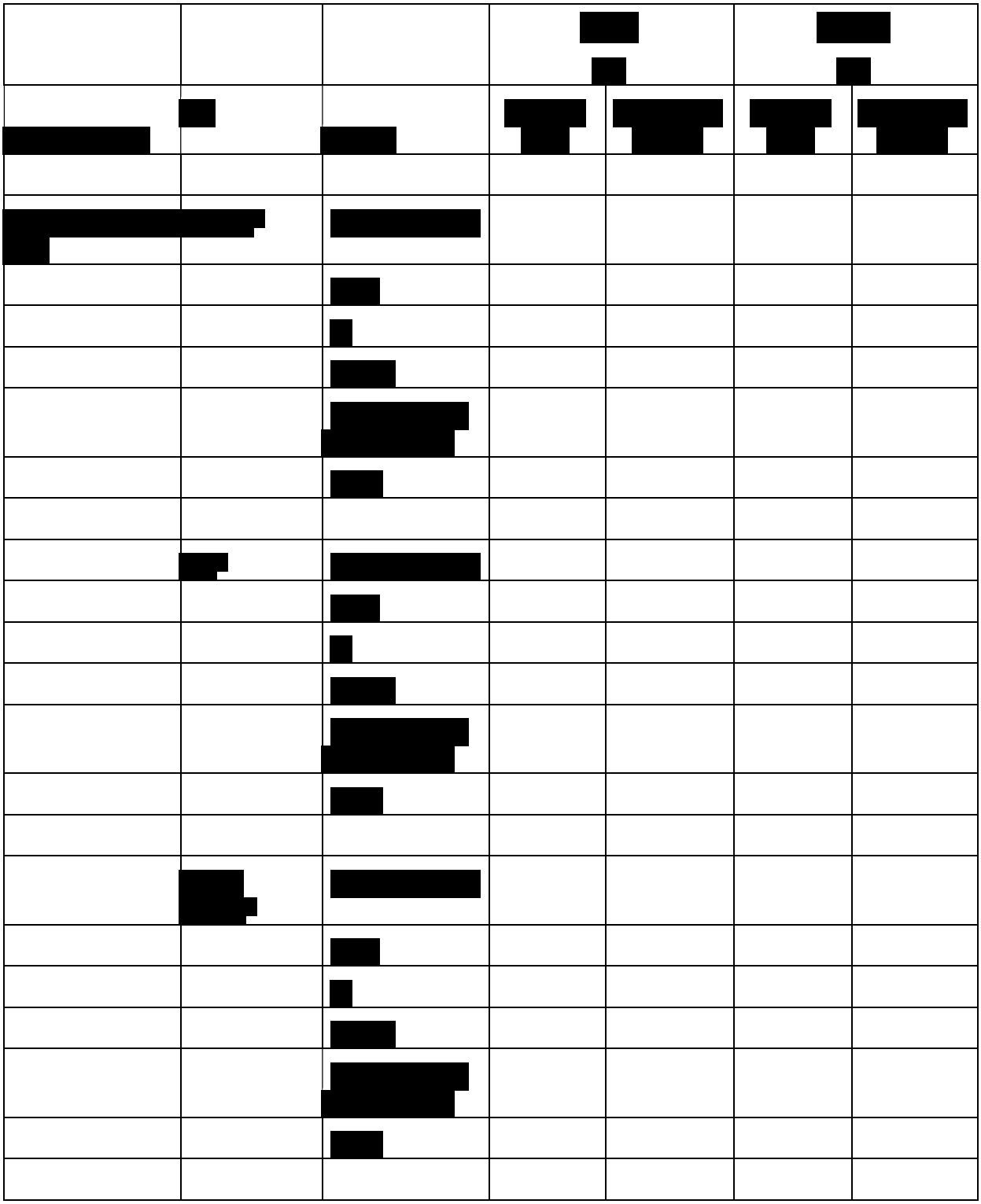

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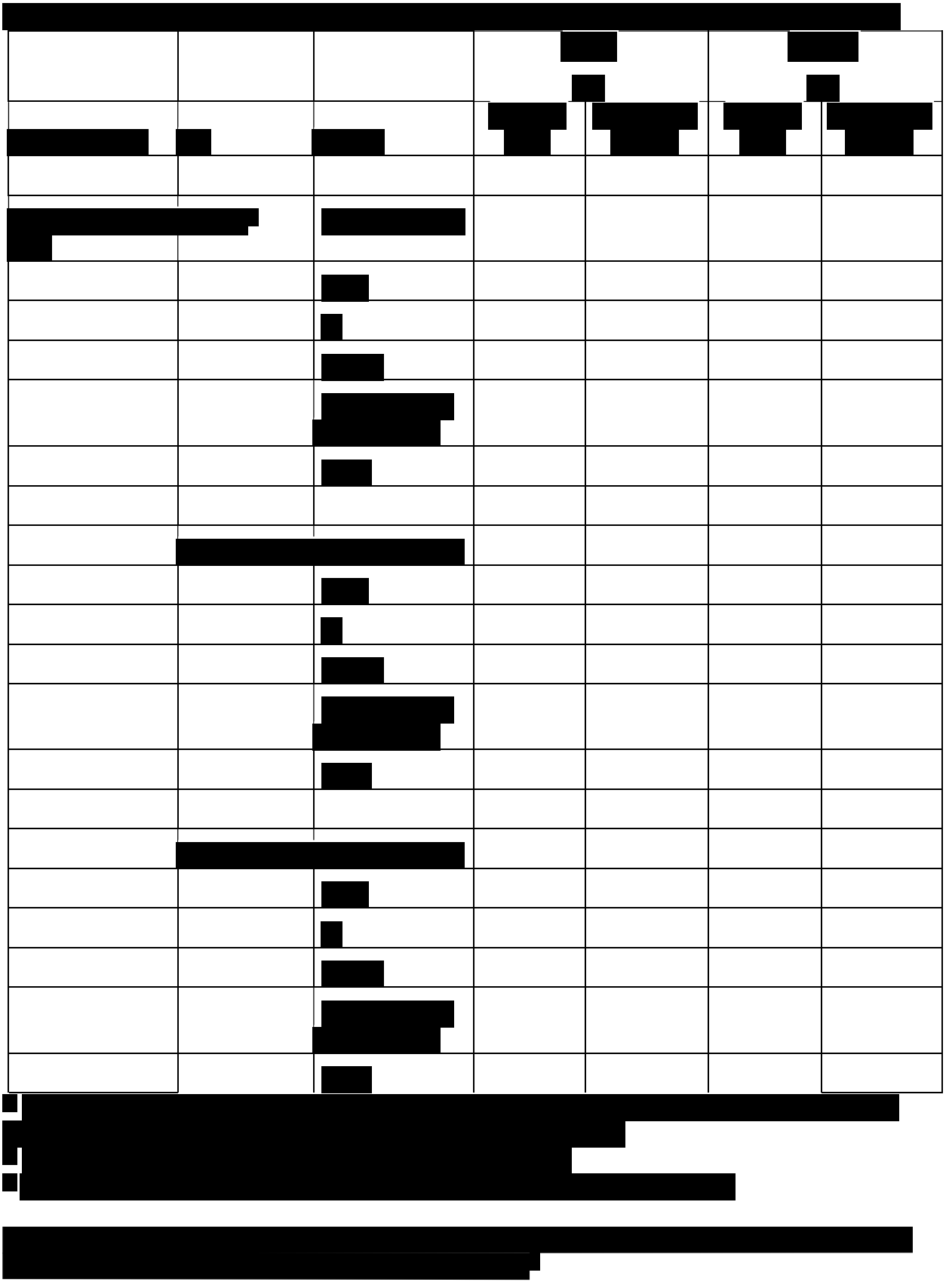

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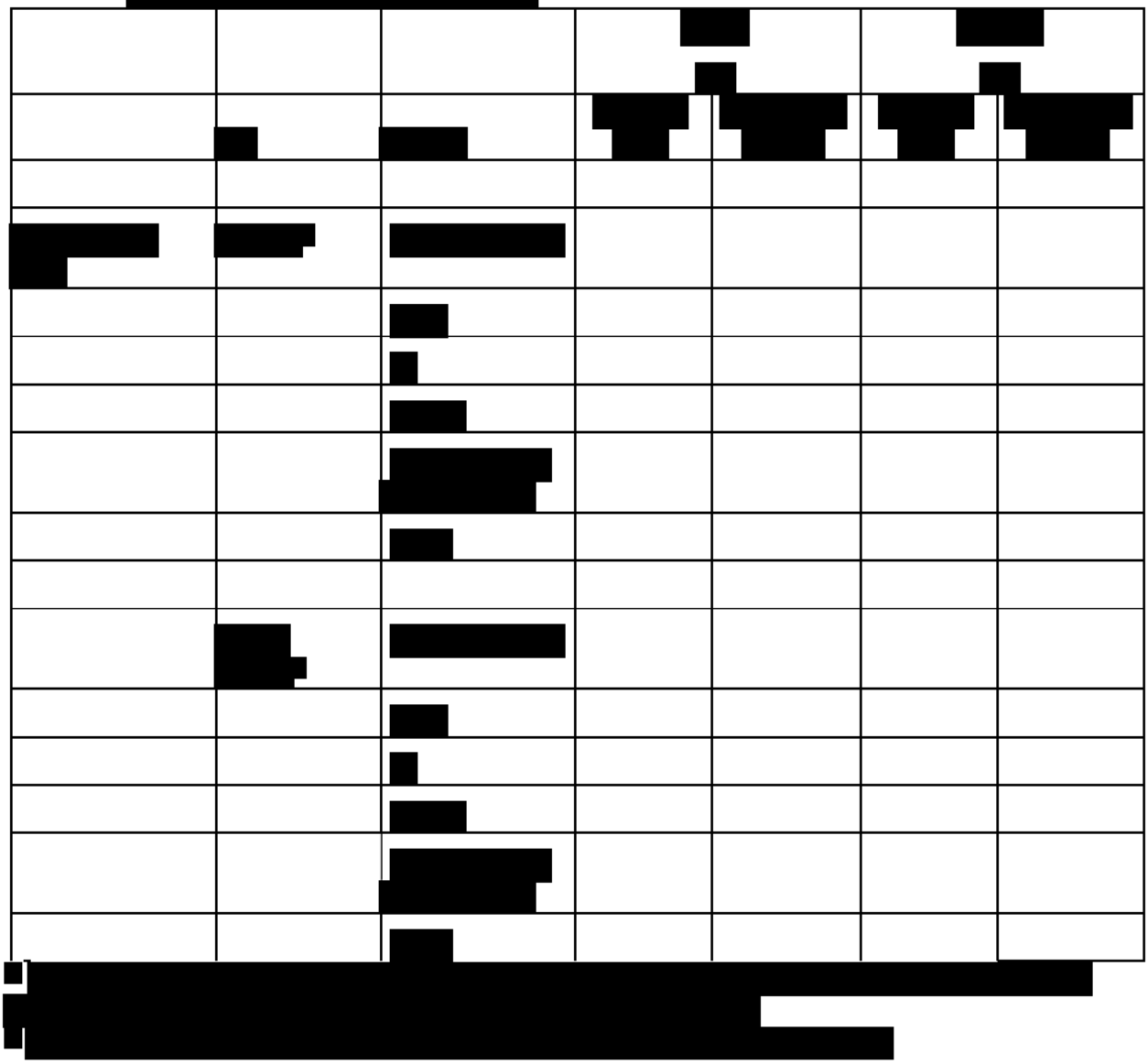

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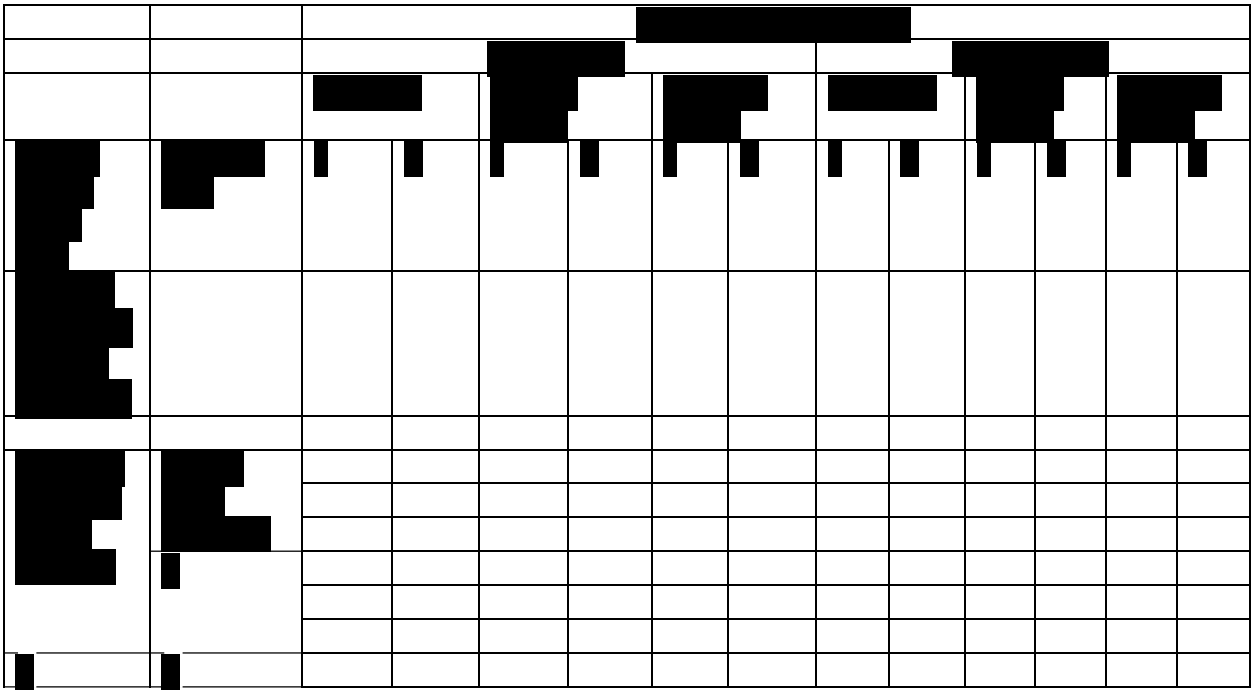

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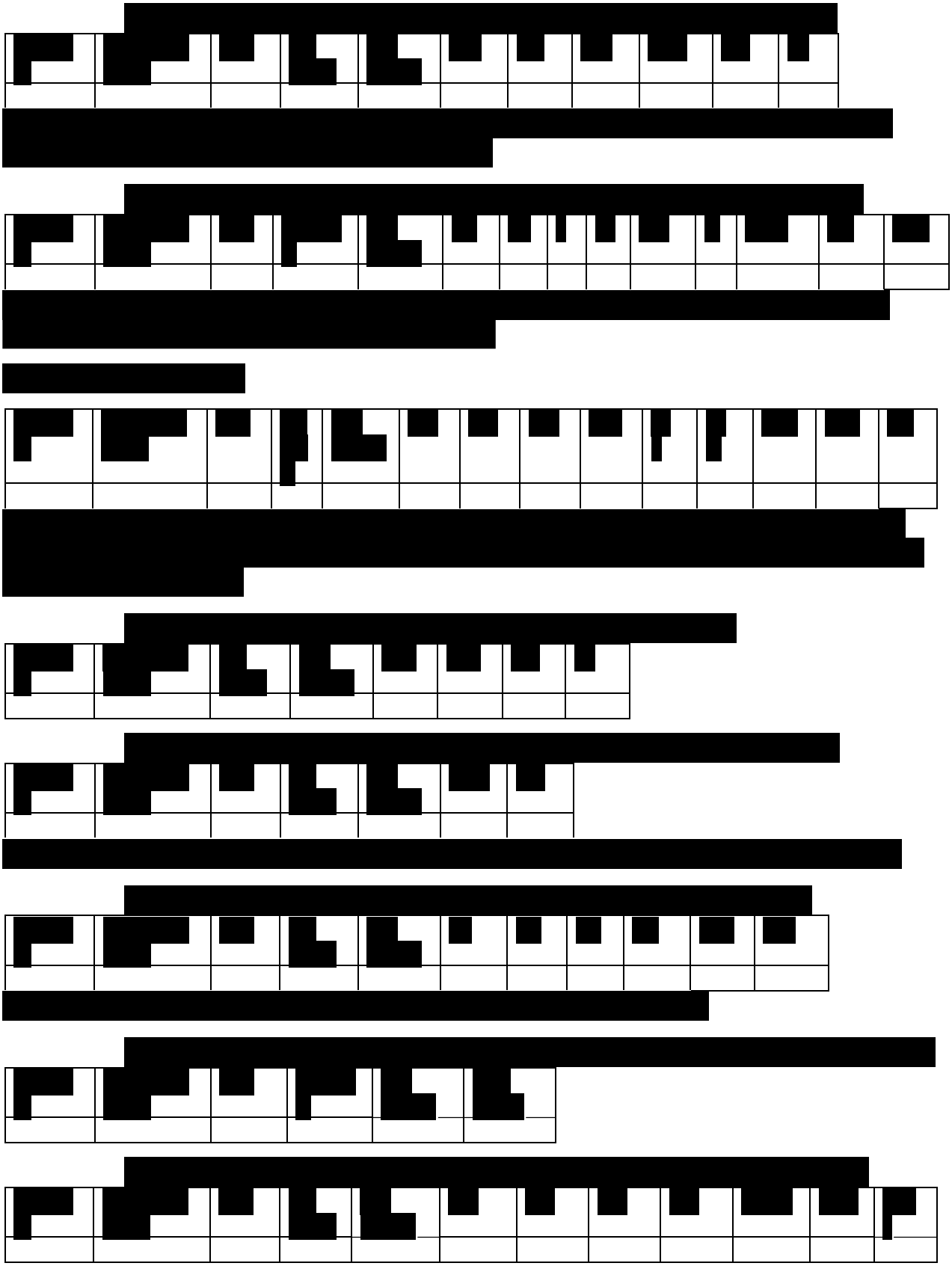

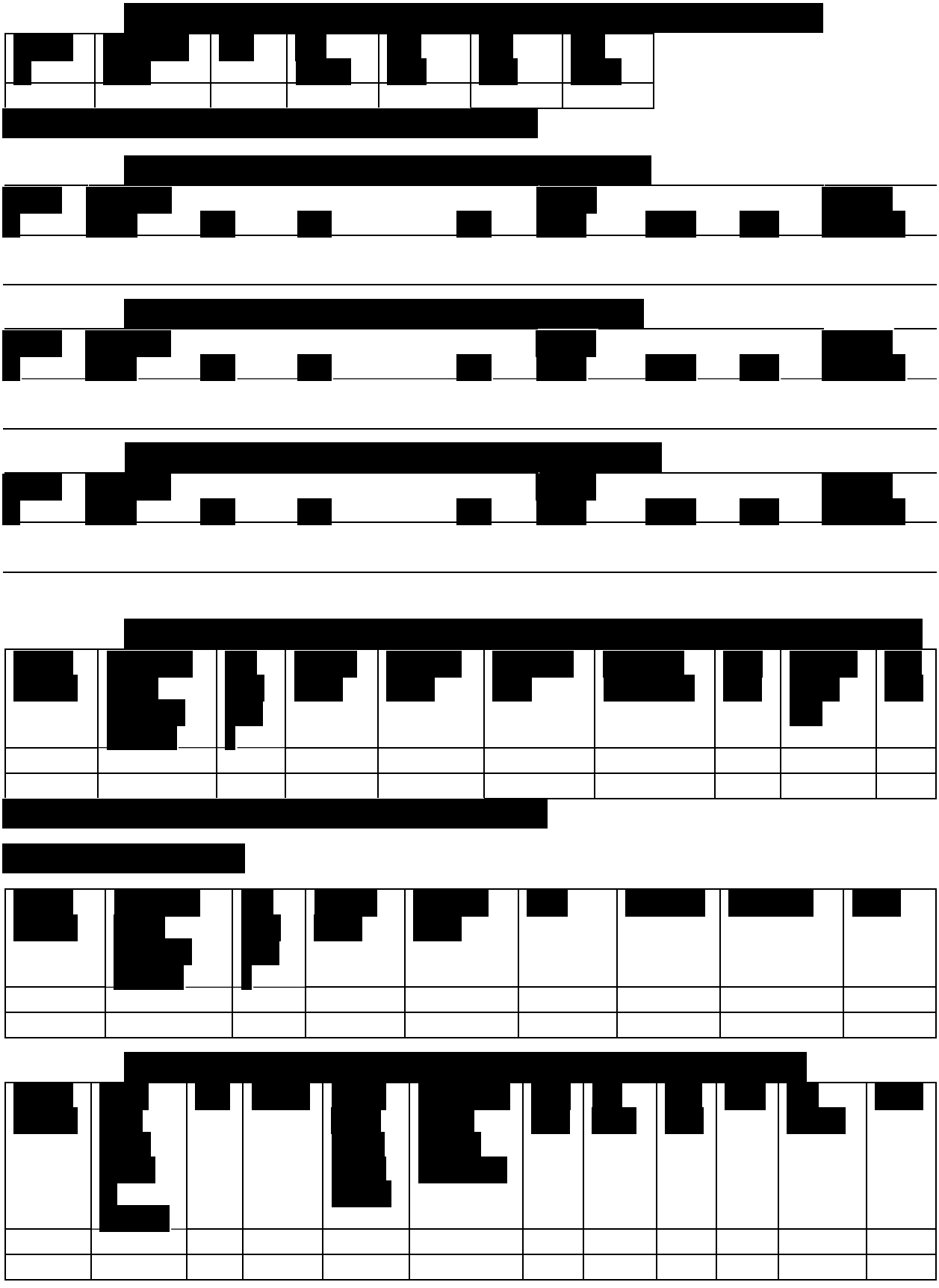

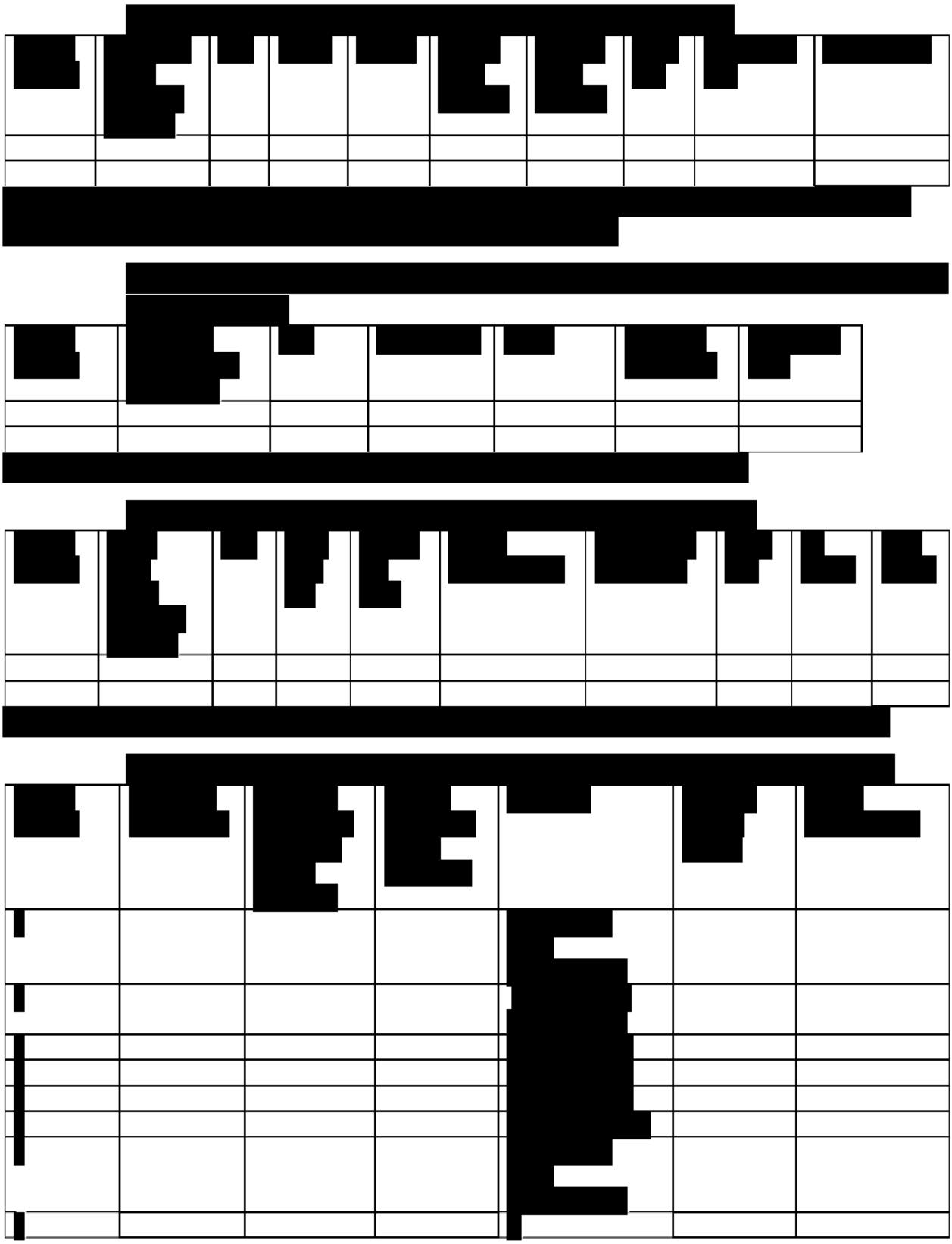

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